Supplementary Information

Catalytic Enantioselective Intramolecular Cyclization of N-Aryl Diazoamides Using Titanium-BINOLate Complex

Takuya Hashimoto, Kumiko Yamamoto, and Keiji Maruoka*

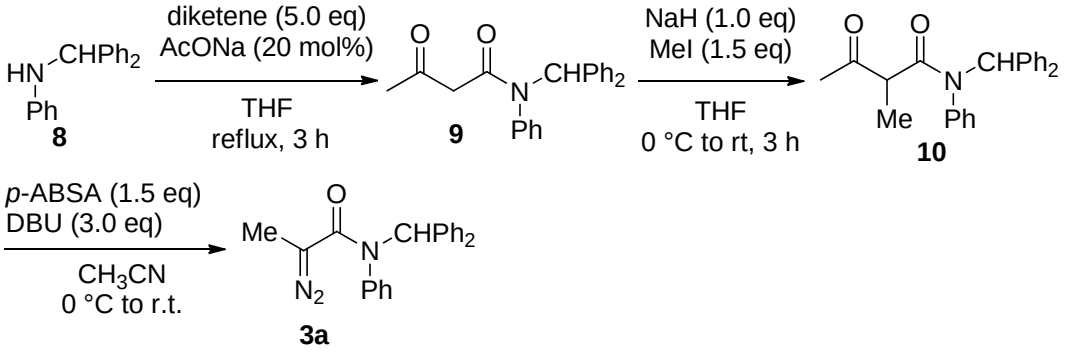
Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto 606-8502, Japan

General Information

Infrared (IR) spectra were recorded on a Shimadzu IRPrestige-21 spectrometer. ^{1}H NMR spectra were measured on a JEOL JNM-FX400 (400 MHz) spectrometer. Data were reported as follows: chemical shifts in ppm from tetramethylsilane as an internal standard in $CDCl_3$, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = double-doublet, dq = double quartet, ddd= double double doublet, m = multiplet, br = broad, and app = apparent) and coupling constants (Hz). ^{13}C NMR spectra were measured on a JEOL JNM-FX400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard. High performance liquid chromatography (HPLC) was performed on Shimadzu 10A instruments at 210 nm or 254 nm using 4.6 nm x 25 cm Daicel Chiralpak and Chiralcel. High-resolution mass spectra (HRMS) were performed on Brucker microTOF. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter. For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. The products were purified by flash column chromatography on silica gel (Kanto Chemical silica gel 60 N, neutral, spherical, 40-50 μm or Merck silica gel 60, 0.040-0.063 mm).

In experiments requiring dry solvent, CH_2Cl_2 was purchased from Kanto Chemical Co. Inc. as “Dehydrated” and further purified by passing through neutral alumina under nitrogen atmosphere. Commercially obtained reagents were used as received.

Representative procedure for the synthesis of diazoamide 3a



To a stirred solution of N-benzhydrylaniline[1] **8** (14.8 mmol, 3.83 g) and sodium acetate (2.95 mmol, 242.0 mg) in THF (30 mL) was added diketene (73.9 mmol, 5.7 mL) at room temperature. After stirring for 3 h at reflux, the mixture was treated with 1 M K_2CO_3 aq. and extracted with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 2:1) to give N-benzhydryl-3-oxo-N-phenylbutanamide **9** as a yellow liquid [98%, 4.96 g].

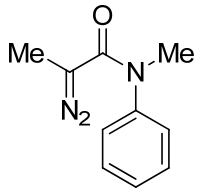
To a stirred solution of **9** (3.0 mmol, 1.05 g) in THF (10 mL) was added sodium hydride (60% dispersion in mineral oil, 3.0 mmol, 120 mg) at 0 °C. After stirring for 15 min, methyl iodide (4.5 mmol, 280 μL) was added to this solution, and the reaction was warmed to room temperature and stirred for 3 h. The mixture was then treated with saturated aqueous NH_4Cl, and the organic layer was extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 4:1) to give N-benzhydryl-2-methyl-3-oxo-N-phenylbutanamide **8** as a white solid [87% (2.61 mmol, 1.57 g)].

To a stirred solution of **10** (2.61 mmol, 1.57 g) and *p*-acetamidobenzenesulfonyl azide (*p*-ABSA) (3.92 mmol, 941 mg) in MeCN (2.6 mL) was added DBU (7.83 mmol, 1.17 mL) at 0 °C. The reaction mixture was then allowed to warm to room temperature and stirred for 2 h. The resulting mixture was poured into H_2O, and extracted with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel (Kanto Chemical silica gel 60N, eluting with hexane/ethyl acetate = 5:1, 1% Et_3N) to give **3a** as a yellow solid [48% (1.26 mmol, 429 mg)].

N-Benzhydryl-2-diazo-N-phenylpropanamide 3a

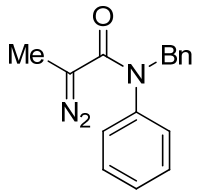
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.10 (14H, m), 6.89 (2H, m), 1.83 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 140.6, 139.2, 129.7, 129.4, 128.8, 128.0, 127.7, 127.2, 65.4, 53.2, 11.5; IR (neat) 2060, 1612, 1593, 1493, 1327, 1179 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{22}H_{19}N_3O$: *m/z* 364.1420 ($[M + Na]^+$), found: *m/z* 364.1416 ($[M + Na]^+$).

2-Diazo-N-methyl-N-phenylpropanamide 1



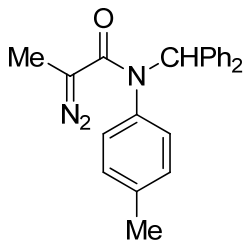
Orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (2H, m), 7.29 (1H, m), 7.21 (2H, m), 3.33 (3H, s), 1.79 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 144.1, 129.7, 127.1, 126.4, 52.6, 38.8, 10.9; IR (neat) 2930, 2060, 1616, 1591, 1352 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{10}H_{11}N_3O$: *m/z* 212.0794 ([M + Na]$^+$), found: *m/z* 212.0796 ([M + Na]$^+$).

N-Benzyl-2-diazo-N-phenylpropanamide 2



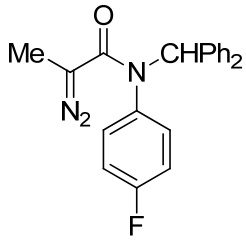
Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.20 (8H, m), 7.07 (2H, m), 4.93 (2H, s), 1.81 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 142.5, 137.6, 129.5, 128.5, 128.3, 127.4, 127.3, 127.2, 54.4, 52.7, 11.2; IR (neat) 2926, 2060, 1614, 1591, 1373, 1323, 1175 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{16}H_{15}N_3O$: *m/z* 288.1107 ([M + Na]$^+$), found: *m/z* 288.1103 ([M + Na]$^+$).

N-Benzhydryl-2-diazo-N-(4-tolyl)propanamide 3b



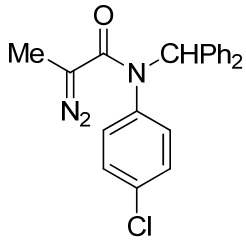
Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.18 (10H, m), 7.14 (1H, s), 6.92 (2H, d, *J* = 8.0 Hz), 6.75 (2H, m), 2.26 (3H, s), 1.83 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 139.3, 137.8, 137.7, 129.7, 129.5, 129.4, 128.0, 127.2, 65.3, 53.0, 21.0, 11.7; IR (neat) 2058, 1612, 1599, 1510, 1327, 1169 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{23}H_{21}N_3O$: *m/z* 378.1577 ([M + Na]$^+$), found: *m/z* 378.1573 ([M + Na]$^+$).

N-Benzhydryl-2-diazo-N-(4-fluorophenyl)propanamide 3c



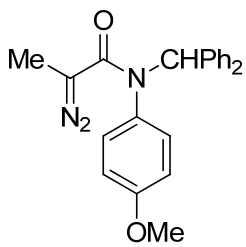
Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.17 (11H, m), 6.85-6.78 (4H, m), 1.85 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 161.8 (d, ^{1}J(^{13}C, ^{19}F) = 249.1 Hz), 139.0, 136.3 (d, ^{4}J(^{13}C, ^{19}F) = 3.3 Hz), 131.6 (d, ^{3}J(^{13}C, ^{19}F) = 8.2 Hz), 129.4, 128.1, 127.4, 115.8 (d, ^{2}J(^{13}C, ^{19}F) = 22.1 Hz), 65.0, 52.9, 11.6; IR (neat) 2058, 1612, 1506, 1325 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{22}H_{18}FN_3O$: *m/z* 382.1326 ([M + Na]$^+$), found: *m/z* 382.1323 ([M + Na]$^+$).

N-Benzhydryl- N-(4-chlorophenyl)-2-diazopropanamide 3d



Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.17 (11H, m), 7.10 (2H, m), 6.79 (2H, m), 1.83 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 139.1, 138.9, 133.5, 130.8, 129.4, 129.1, 128.2, 127.4, 65.1, 53.3, 11.4; IR (neat) 2060, 1614, 1489, 1321, 1167 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{22}H_{18}ClN_3O$: *m/z* 398.1031 ([M + Na]$^+$), found: *m/z* 398.1034 ([M + Na]$^+$).

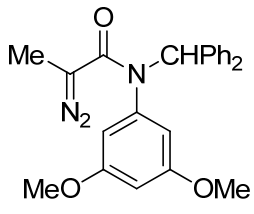
N-Benzhydryl-2-diazo-N-(4-methoxyphenyl)propanamide 3e



Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.18 (11H, m), 6.76 (2H, m), 6.62 (2H, m), 3.73 (3H, s), 1.86 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 159.2, 139.2,

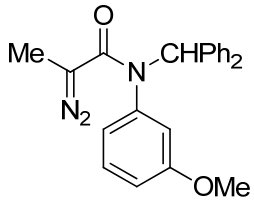
132.7, 131.4, 129.5, 127.9, 127.1, 113.8, 65.0, 55.3, 52.6, 11.9; IR (neat) 2054, 1611, 1508, 1337, 1248, 1169 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{23}H_{21}N_3O_2$: *m/z* 394.1526 ([M + Na]$^+$), found: *m/z* 394.1528 ([M + Na]$^+$).

N-Benzhydryl-2-diazo-N-(3,5-dimethoxyphenyl)propanamide 3f



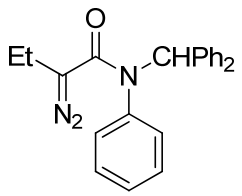
Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.21 (10H, m), 7.12 (1H, s), 6.27 (1H, t, *J* = 2.2 Hz), 6.03 (2H, d, *J* = 2.2 Hz), 3.56 (6H, s), 1.86 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 160.6, 142.0, 139.2, 129.4, 128.0, 127.2, 108.2, 100.0, 65.4, 55.3, 53.5, 11.5; IR (neat) 2060, 1589, 1456, 1339, 1206, 1155 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{24}H_{23}N_3O_3$: *m/z* 424.1632 ([M + Na]$^+$), found: *m/z* 424.1633 ([M + Na]$^+$).

N-Benzhydryl-2-diazo-N-(3-methoxyphenyl)propanamide 3g



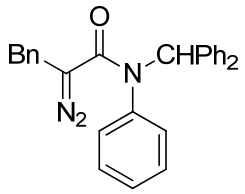
Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.20 (10H, m), 7.15 (1H, s), 7.04 (1H, dd, *J* = 8.1, 8.1 Hz), 6.71 (1H, ddd, *J* = 8.3, 2.5, 0.7 Hz), 6.54 (1H, m), 6.36 (1H, dd, *J* = 2.2, 2.2 Hz), 3.57 (3H, s), 1.84 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 159.8, 141.5, 139.2, 129.43, 129.38, 128.0, 127.2, 122.2, 115.3, 113.6, 65.4, 55.2, 53.4, 11.5; IR (neat) 2060, 1614, 1593, 1489, 1323, 1175, 1163 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{23}H_{21}N_3O_2$: *m/z* 394.1526 ([M + Na]$^+$), found: *m/z* 394.1525 ([M + Na]$^+$).

N-Benzhydryl-2-diazo-N-phenylbutanamide 3h



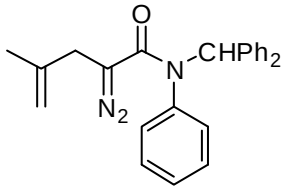
Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.10 (14H, m), 6.90 (2H, m), 2.30 (2H, q, *J* = 7.4 Hz), 1.01 (3H, t, *J* = 7.5 Hz) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 140.6, 139.3, 129.7, 129.4, 128.9, 128.0, 127.7, 127.2, 65.4, 58.3, 18.7, 11.5; IR (neat) 2058, 1618, 1589, 1350, 1302 HRMS (ESI) exact mass calcd for $C_{23}H_{21}N_3O$: *m/z* 378.1577 ([M + Na]$^+$), found: *m/z* 378.1567 ([M + Na]$^+$).

N-Benzhydryl-2-diazo-N,3-diphenylpropanamide 3i



Orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.07 (19H, m), 6.85 (2H, m), 3.58 (2H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 140.2, 139.1, 137.5, 129.6, 129.3, 128.7, 128.4, 128.3, 127.9, 127.7, 127.1, 126.7, 65.4, 58.0, 31.6; IR (neat) 2062, 1616, 1593, 1493, 1350, 1300, 1179 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{28}H_{23}N_3O$: *m/z* 440.1733 ([M + Na]$^+$), found: *m/z* 440.1727 ([M + Na]$^+$).

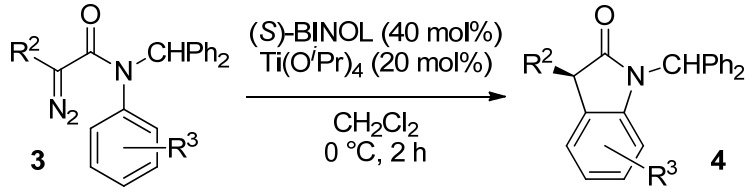
N-Benzhydryl-2-diazo-4-methyl-N-phenylpent-4-enamide 3j



Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.10 (13H, m), 6.91 (2H, m), 4.79 (1H, s), 4.69 (1H, s), 2.97 (2H, s), 1.68 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 140.8, 140.5, 139.3, 129.8, 129.4, 128.9, 128.0, 127.9, 127.2, 112.8, 65.5,

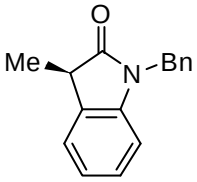
56.2, 33.9, 21.6; IR (neat) 2060, 1616, 1587, 1493, 1346, 1298 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{25}H_{23}N_3O$: *m/z* 382.1914 ($[M + H]^+$), found: *m/z* 382.1906 ($[M + H]^+$).

General procedure for the titanium-BINOLate catalyzed asymmetric C-H functionalization using N-aryl diazoamides (Table 2)



To a stirred solution of (*S*)-BINOL (0.10 mmol, 28.6 mg) in CH_2Cl_2 (1.0 mL) was added $Ti(O^iPr)_4$ (0.05 mmol, 14.8 μL) at room temperature. The mixture was stirred for 1 h and cooled to 0 °C. To this catalyst solution was added N-aryl α-diazoamide **3** (0.25 mmol). After the full consumption of **3** which was monitored by ESI-MS, the residue was directly charged to column chromatography on silica gel (Merck silica gel 60) with a dry ice cooling jacket to give oxindole **4**.[2]

(*R*)-1-Benzyl-3-methylindolin-2-one (Table 1, entry 1)

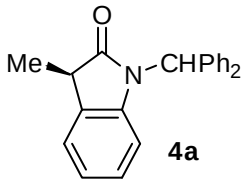


Prepared according to the general procedure with **2** (0.25 mmol, 66.3 mg) over the course of 20 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/acetone = 10:1 (0.5% AcOH) and 2nd run with CH_2Cl_2/ethyl acetate = 100:1 (0.5% AcOH)) to give (*R*)-1-benzyl-3-methylindolin-2-one as a white solid [52% (30.9 mg), 70% ee].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD3, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, retention time; 17.4 min (minor) and 19.3 min (major)).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.23 (6H, m), 7.15 (1H, t, *J* = 7.7 Hz), 7.02 (1H, t, *J* = 7.4 Hz), 6.71 (1H, d, *J* = 8.0 Hz), 4.91 (2H, s), 3.53 (1H, q, *J* = 7.7 Hz), 1.54 (3H, d, *J* = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.7, 143.1, 136.0, 130.7, 128.7, 127.8, 127.5, 127.3, 123.6, 122.4, 109.0, 43.7, 40.6, 15.6; IR (neat) 1711, 1614, 1487, 1356 cm^{-1}; HRMS(ESI) exact mass calcd for $C_{16}H_{15}NO$: *m/z* 260.1046 ([M + Na]$^+$), found: *m/z* 260.1044 [M +Na]$^+$); $[\alpha]_D^{29}$ +16.7 (*c* = 1.00, $CHCl_3$).

(*R*)-1-Benzhydryl-3-methylindolin-2-one 4a



4a

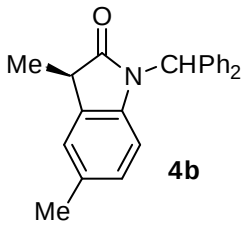
Prepared according to the general procedure with **3a** (0.25 mmol, 85.4 mg) at 0 °C over the course of 2 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/acetone = 10:1 (0.5% AcOH) and 2nd run with CH_2Cl_2/hexane = 4:1 (0.5% AcOH)) to give **4a** as a white solid [77% (60.6 mg), 96% ee].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD3, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, retention time; 20.8 min (minor) and 23.6 min (major)).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.22 (11H, m), 7.02 (1H, s), 6.99-6.94 (2H, m), 6.43 (1H, m), 3.54 (1H, q, *J* = 7.7 Hz), 1.53 (3H, d, *J* = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.8, 142.6, 137.9, 137.8, 130.7, 128.51, 128.47, 128.4, 127.7, 127.6, 127.2, 123.5, 122.1, 111.8, 58.0, 40.2, 15.9; IR (neat) 1709, 1609, 1481, 1466, 1350, 1331 cm^{-1}; HRMS(ESI) exact mass calcd for $C_{22}H_{19}NO$: *m/z* 336.1359 ([M + Na]$^+$), found: *m/z*

336.1361 [M +Na]$^+$); $[\alpha]_D^{29}$ +29.4 (*c* = 1.00, $CHCl_3$).

(*R*)-1-Benzhydryl-3,5-dimethylindolin-2-one 4b

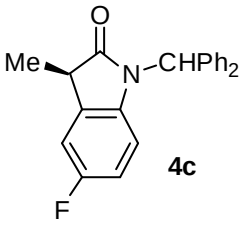


4b

Prepared according to the general procedure with **3b** (0.25 mmol, 88.9 mg) over the course of 2 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/acetone = 10:1 (0.5% AcOH) and 2nd run with CH_2Cl_2/hexane = 4:1 (0.5% AcOH)) to give **4b** as a white solid [76% (62.3 mg), 93% ee].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD3, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, retention time; 12.0 min (minor) and 16.3 min (major)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.24 (10H, m), 7.05 (1H, s), 7.01 (1H, s), 6.76 (1H, d, *J* = 8.0 Hz), 6.30 (1H, d, *J* = 8.0 Hz), 3.51 (1H, q, *J* = 7.5 Hz), 2.27 (3H, s), 1.51 (3H, d, *J* = 7.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.8, 140.1, 138.0, 137.9, 131.6, 130.8, 128.5, 128.4, 127.62, 127.58, 127.5, 124.3, 111.5, 57.9, 40.3, 20.9, 15.9; IR (neat) 1709, 1597, 1487, 1327, 1196 cm^{-1}; HRMS(ESI) exact mass calcd for $C_{23}H_{21}NO$: *m/z* 350.1515 ([M + Na]$^+$), found: *m/z* 350.1504 [M +Na]$^+$); $[\alpha]_D^{30}$ +35.1 (*c* = 1.00, $CHCl_3$).

(*R*)-1-Benzhydryl-5-fluoro-3-methylindolin-2-one 4c

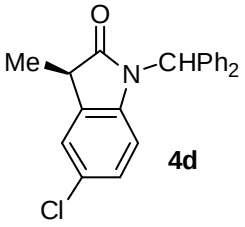


4c

Prepared according to the general procedure with **3c** (0.25 mmol, 89.9 mg) over the course of 6 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/acetone = 10:1 (0.5% AcOH) and 2nd run with CH_2Cl_2/hexane = 4:1 (0.5% AcOH)) to give **4c** as a white solid [59% (49.2 mg), 94% ee].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, retention time; 12.8 min (minor) and 17.0 min (major)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.22 (10H, m), 7.02 (1H, s), 6.97 (1H, m), 6.66 (1H, m), 6.32 (1H, dd, *J* = 8.7 Hz, ^4J(H,F) = 4.4 Hz), 3.54 (1H, q, *J* = 7.6 Hz), 1.53 (3H, d, *J* = 7.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 158.9 (d, ^1J(^{13}C, ^{19}F) = 240.9 Hz), 138.4 (d, ^4J(^{13}C, ^{19}F) = 2.5 Hz), 137.64, 137.57, 132.5 (d, ^3J(^{13}C, ^{19}F) = 8.2 Hz), 128.6, 128.4, 128.3, 127.8 (d, ^3J(^{13}C, ^{19}F) = 3.3 Hz), 113.6 (d, ^2J(^{13}C, ^{19}F) = 22.9 Hz), 112.3, 112.2, 111.5 (d, ^2J(^{13}C, ^{19}F) = 24.6 Hz), 58.1, 40.6 (d, ^4J(^{13}C, ^{19}F) = 1.6 Hz), 15.9; IR (neat) 1713, 1607, 1483, 1325, 1190, 1171 cm^{-1}; HRMS(ESI) exact mass calcd for $C_{22}H_{18}FNO$: *m/z* 354.1265 ([M + Na]$^+$), found: *m/z* 354.1270 [M +Na]$^+$); $[\alpha]_D^{30}$ +25.3 (*c* = 1.00, $CHCl_3$).

(*R*)-1-Benzhydryl-5-chloro-3-methylindolin-2-one 4d



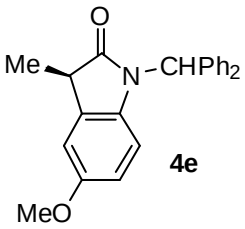
4d

Prepared according to the general procedure with **3d** (0.25 mmol, 94.0 mg) over the course of 2 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/acetone = 10:1 (0.5% AcOH) and 2nd run with CH_2Cl_2/hexane = 4:1 (0.5% AcOH)) to give **4d** as a white solid [58% (50.5 mg), 96% ee].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD3, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, retention time; 14.0 min (minor) and 19.8 min (major)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.21 (11H, m), 7.01 (1H, s), 6.93 (1H, m), 6.32 (1H, d, *J* = 8.5 Hz), 3.54

(1H, q, J = 7.5 Hz), 1.52 (3H, d, J = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 141.1, 137.5, 137.4, 132.5, 128.6, 128.4, 128.3, 127.85, 127.82, 127.6, 127.2, 124.0, 112.6, 58.1, 40.3, 15.8; IR (neat) 1717, 1609, 1477, 1323, 1169 cm^{-1}; HRMS(ESI) exact mass calcd for $C_{22}H_{18}ClNO$: *m/z* 370.0969 ([M + Na]$^+$), found: *m/z* 370.0975 [M +Na]$^+$); $[\alpha]_D^{28}$ +37.2 (*c* = 1.0, $CHCl_3$).

(*R*)-1-Benzhydryl-5-methoxy-3-methylindolin-2-one 4e



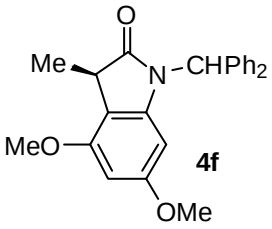
4e

Prepared according to the general procedure with **3e** (0.25 mmol, 92.9 mg) at –20 °C over the course of 2 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/acetone = 10:1 (0.5% AcOH) and 2nd run with isopropanol (0.5% AcOH)) to give **4e** as a white solid [63% (55.9 mg), 92% ee].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD3, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, retention time; 16.5 min (minor) and 22.8 min (major)).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.24 (10H, m), 7.01 (1H, s), 6.84 (1H, dd, J = 2.5, 0.8 Hz), 6.49 (1H, dd, J = 8.7, 2.7 Hz), 6.30 (1H, d, J = 8.5 Hz), 3.72 (3H, s), 3.52 (1H, q, J = 7.6 Hz), 1.52 (3H, d, J = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 155.5, 137.93, 137.86, 135.9, 132.2, 128.49, 128.47, 128.4, 127.63, 127.60, 112.1, 111.5, 110.9, 57.9, 55.6, 40.6, 16.0; IR (neat) 1705, 1597, 1487, 1454, 1329, 1196, 1032 cm^{-1}; HRMS(ESI) exact mass calcd for $C_{23}H_{21}NO_2$: *m/z* 366.1465 ([M + Na]$^+$), found: *m/z* 360.1457 [M +Na]$^+$); $[\alpha]_D^{28}$ +34.9 (*c* = 1.0, $CHCl_3$).

(*R*)-1-Benzhydryl-4,6-dimethoxy-3-methylindolin-2-one 4f



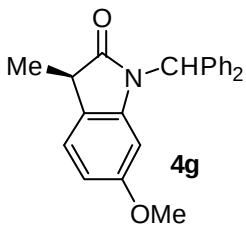
4f

Prepared according to the general procedure with **3f** (0.25 mmol, 100.4 mg) at –30 °C for 8 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 5:1 (0.5% AcOH)) to give **4f** as a white solid [92% (86.2 mg), 92% ee].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD3, hexane/2-propanol = 20:1, flow rate = 0.5 mL/min, retention time; 15.9 min (minor) and 18.5 min (major)).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.25 (10H, m), 6.98 (1H, s), 6.09 (1H, d, J = 1.9 Hz), 5.64 (1H, d, J = 2.2 Hz), 3.80 (3H, s), 3.54 (1H, q, J = 7.4 Hz), 3.47 (3H, s), 1.51 (3H, d, J = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.8, 160.4, 156.4, 144.4, 138.10, 138.05, 128.52, 128.49, 128.36, 127.63, 127.61, 109.1, 92.3, 91.8, 58.1, 55.31, 55.26, 38.9, 15.1; IR (neat) 1715, 1614, 1449, 1204, 1152 cm^{-1}; HRMS(ESI) exact mass calcd for $C_{24}H_{23}NO_3$: *m/z* 396.1570 ([M + Na]$^+$), found: *m/z* 396.1569 [M +Na]$^+$); $[\alpha]_D^{28}$ +26.4 (*c* = 1.00, $CHCl_3$).

(*R*)-1-Benzhydryl-6-methoxy-3-methylindolin-2-one 4g



4g

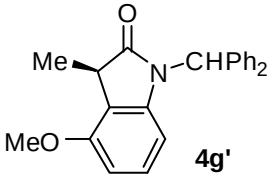
Prepared according to the general procedure with **3g** (0.25 mmol, 92.9 mg) at –20 °C for 2 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1 (0.5% AcOH) to isolate **4g'** and 2nd run with CH_2Cl_2/hexane = 4:1 (0.5% AcOH) to isolate **4g**) to give **4g** as a white solid [64%

(0.160 mg), 93% ee] and **4g'** as a white solid [9% (8.0 mg), 95% ee].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD3, hexane/2-propanol = 30:1, flow rate = 0.5 mL/min, retention time; 19.2 min (minor) and 17.6 min (major)).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.25 (10H, m), 7.10 (1H, dd, *J* = 8.1, 0.8 Hz), 7.00 (1H, s), 6.48 (1H, dd, *J* = 8.1, 2.3 Hz), 6.01 (1H, d, *J* = 2.4 Hz), 3.53 (3H, s), 3.49 (1H, q, *J* = 7.6 Hz), 1.49 (3H, d, *J* = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.5, 159.1, 143.8, 137.9, 137.8, 128.6, 128.5, 128.4, 127.71, 127.67, 123.8, 122.7, 106.6, 99.5, 58.1, 55.3, 39.7, 16.2; IR (neat) 1715, 1626, 1597, 1497, 1452, 1211, 1165 cm^{-1}; HRMS(ESI) exact mass calcd for $C_{23}H_{21}NO_2$: *m/z* 366.1465 ([M + Na]$^+$), found: *m/z* 366.1467 [M +Na]$^+$); $[\alpha]_D^{29}$ +30.1 (*c* = 1.00, $CHCl_3$).

(*R*)-1-Benzhydryl-4-methoxy-3-methylindolin-2-one 4g'

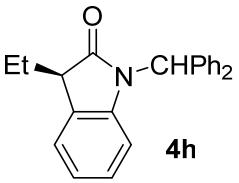


4g'

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD3, hexane/2-propanol = 30:1, flow rate = 0.5 mL/min, retention time; 15.9 min (minor) and 18.2 min (major)).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.25 (10H, m), 6.99 (1H, s), 6.94 (1H, m), 6.52 (1H, d, *J* = 8.5 Hz), 6.09 (1H, d, *J* = 8.0 Hz), 3.83 (3H, s), 3.59 (1H, q, *J* = 7.5 Hz), 1.55 (3H, d, *J* = 7.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.2, 155.9, 143.8, 138.03, 137.98, 128.48, 128.46, 128.4, 128.3, 127.60, 127.57, 117.0, 105.4, 105.0, 58.0, 55.3, 39.3, 14.8; IR (neat) 1713, 1603, 1466, 1261 cm^{-1}; HRMS(ESI) exact mass calcd for $C_{23}H_{21}NO_2$: *m/z* 366.1465 ([M + Na]$^+$), found: *m/z* 366.1460 [M +Na]$^+$); $[\alpha]_D^{30}$ +38.5 (*c* = 0.50, $CHCl_3$).

(*R*)-1-Benzhydryl-3-ethylindolin-2-one 4h



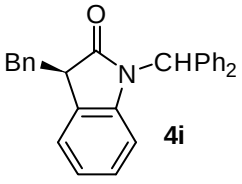
4h

Prepared according to the general procedure with **3h** (0.25 mmol, 88.9 mg) over the course of 2 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/acetone = 10:1 (0.5% AcOH) and 2nd run with CH_2Cl_2/hexane = 4:1 (0.5% AcOH)) to give **4h** as a white solid [61% (49.8 mg), 94% ee].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD3, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, retention time; 11.8 min (minor) and 15.1 min (major)).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.21 (11H, m), 7.05 (1H, s), 6.98-6.94 (2H, m), 6.43 (1H, m), 3.55 (1H, t, *J* = 5.4 Hz), 2.09 (2H, m), 0.85 (3H, t, *J* = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 143.3, 137.9, 128.9, 128.49, 128.47, 128.4, 127.64, 127.59, 127.2, 123.7, 121.9, 111.7, 58.0, 46.2, 24.0, 9.8; IR (neat) 1709, 1609, 1481, 1466, 1352 cm^{-1}; HRMS(ESI) exact mass calcd for $C_{23}H_{21}NO$: *m/z* 350.1515 ([M + Na]$^+$), found: *m/z* 350.1508 [M +Na]$^+$); $[\alpha]_D^{18}$ +17.9 (*c* = 1.0, $CHCl_3$).

(*R*)-1-Benzhydryl-3-benzylindolin-2-one 4i



4i

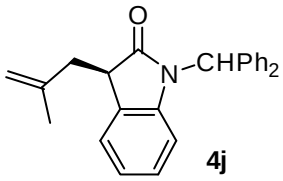
Prepared according to the general procedure with **3i** (0.25 mmol, 104.4 mg) in CH_2Cl_2 (0.30 mL) over the course of 2 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/acetone = 10:1 (0.5% AcOH) and 2nd

run with CH_2Cl_2/hexane = 4:1 (0.5% AcOH)) to give **4i** as a white solid [74% (72.3 mg), 85% ee].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD3, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, retention time; 20.5 min (minor) and 24.8 min (major)).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.13 (11H, m), 7.09-7.05 (3H, m), 6.93-6.88 (3H, m), 6.72 (2H, d, *J* = 7.7 Hz), 6.25 (1H, m), 3.87 (1H, dd, *J* = 7.0, 4.4 Hz), 3.44 (1H, dd, *J* = 13.5, 4.4 Hz), 3.27 (1H, dd, *J* = 13.5, 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 143.0, 137.8, 137.2, 136.9, 129.8, 128.49, 128.47, 128.3, 128.2, 128.1, 127.6, 127.3, 127.2, 126.6, 124.2, 121.7, 111.8, 57.8, 46.7, 36.4; IR (neat) 1709, 1611, 1495, 1481, 1466, 1454 cm^{-1}; HRMS(ESI) exact mass calcd for $C_{28}H_{23}NO$: *m/z* 412.1672 ([M + Na]$^+$), found: *m/z* 412.1671 [M +Na]$^+$); $[\alpha]_D^{28}$ +82.9 (*c* = 1.00, $CHCl_3$).

(*R*)-1-Benzhydryl-3-(methallyl)indolin-2-one 4j



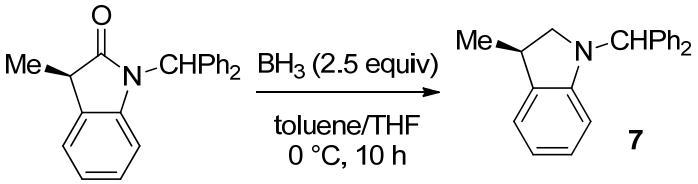
4j

Prepared according to the general procedure with **3j** (0.25 mmol, 95.4 mg) over the course of 2 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/acetone = 10:1 (0.5% AcOH) and 2nd run with CH_2Cl_2/hexane = 4:1 (0.5% AcOH)) to give **4j** as a white solid [63% (55.9 mg), 92% ee].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD3, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, retention time; 19.7 min (minor) and 30.0 min (major)).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.23 (11H, m), 7.03 (1H, s), 6.98-6.90 (2H, m), 6.45 (1H, d, *J* = 7.7 Hz), 4.86 (1H, s), 4.76 (1H, s), 3.68 (1H, dd, *J* = 9.2, 4.4 Hz), 2.86 (1H, dd, *J* = 14.1, 4.0 Hz), 2.46 (1H, dd, *J* = 14.3, 9.2 Hz), 1.76 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.7, 142.8, 141.8, 137.79, 137.76, 129.0, 128.50, 128.46, 127.7, 127.6, 127.2, 124.4, 121.8, 113.8, 111.7, 58.2, 43.4, 39.1, 22.4; IR (neat) 1711, 1609, 1464, 1352, 1221 cm^{-1}; HRMS(ESI) exact mass calcd for $C_{25}H_{23}NO$: *m/z* 376.1672 ([M + Na]$^+$), found: *m/z* 376.1662 [M +Na]$^+$); $[\alpha]_D^{26}$ +20.1 (*c* = 1.00, $CHCl_3$).

Synthesis of (*R*)-1-benzhydryl-3-methylindoline 7 via the borane reduction of 4a (eq. 1)



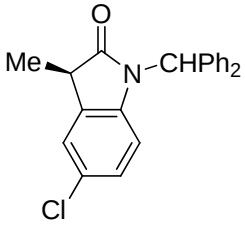
4a (96% ee) 45%, 96% ee

To a stirred solution of **4a** (0.141 mmol, 44.2 mg; 96% ee) in toluene (2.0 mL) was added a 0.95 M THF solution of BH_3·THF (0.353 mmol, 371 μL) at 0 °C. The reaction solution was stirred for 10 h at 0 °C and poured into saturated NH_4Cl aq. The organic layer was extracted with ethyl acetate, dried over Na_2SO_4 and concentrated. The residue was purified by preparative thin layer chromatography (eluting with hexane/acetone = 30:1) to give **7** as a colorless oil [45% (19.0 mg), 96% ee].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak IC3, hexane/2-propanol = 1000:1, flow rate = 0.5 mL/min, retention time; 12.9 min (major) and 14.0 min (minor)).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.22 (10H, m), 7.04 (1H, d, *J* = 7.3 Hz), 6.92 (1H, app t, *J* = 7.6 Hz), 6.65 (1H, m), 6.18 (1H, d, *J* = 8.0 Hz), 5.52 (1H, s), 3.36-3.22 (2H, m), 2.75 (1H, app t, *J* = 8.0 Hz), 2.75 (3H, d, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 141.6, 141.1, 135.4, 128.7, 128.43, 128.37, 128.2, 127.21, 127.17, 127.1, 122.9, 117.5, 108.1, 66.5, 59.5, 34.9, 18.6; IR (neat) 1603, 1487, 1452, 1240 cm^{-1}; HRMS(ESI) exact mass calcd for $C_{22}H_{21}N$: *m/z* 300.1747 ($[M + H]^+$), found: *m/z* 300.1744 $[M + H]^+$); $[\alpha]_D^{27}$ –132.9 (*c* = 1.00, $CHCl_3$).

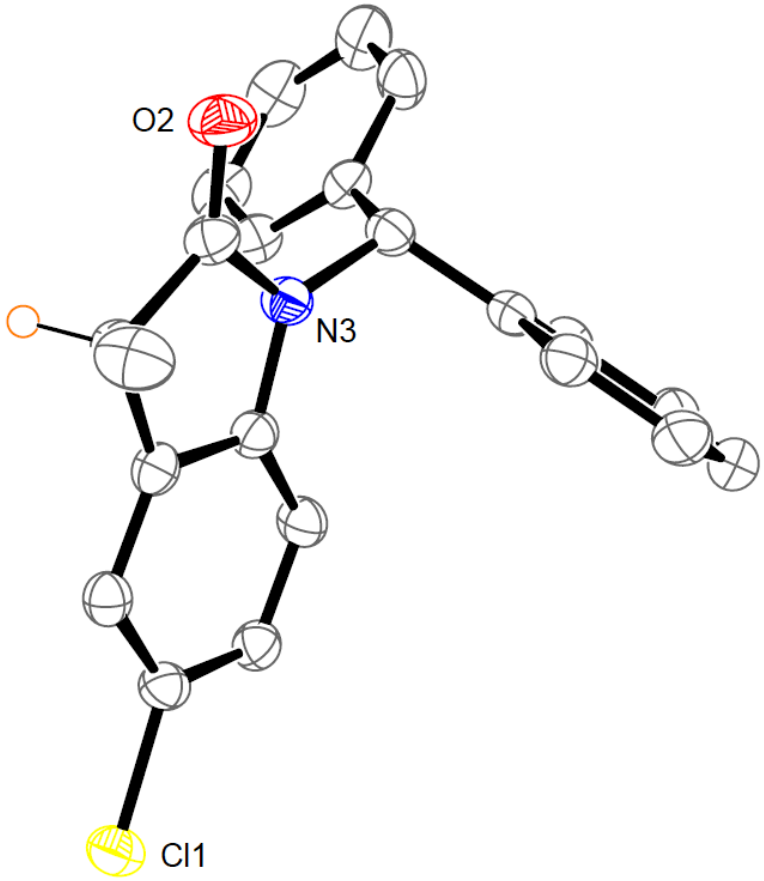
X-ray crystallographic analysis of 4d



The product was recrystallized from hexane/CH_2Cl_2. The single crystal was mounted on a MicroMesh™ (MiTeGen). Data of X-ray diffraction were collected by a Rigaku RAXIS-RAPID Imaging Plate two-dimensional area detector using graphite-monochromated CuKa (l = 1.54187 Å) to a maximam 2θ value of 136.5°. The crystal structure was solved by the direct methods and refined by the full-matrix least squares using the program SHELXL-97.[3] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined by using the riding model. The crystallographic data were summarized in the following table.

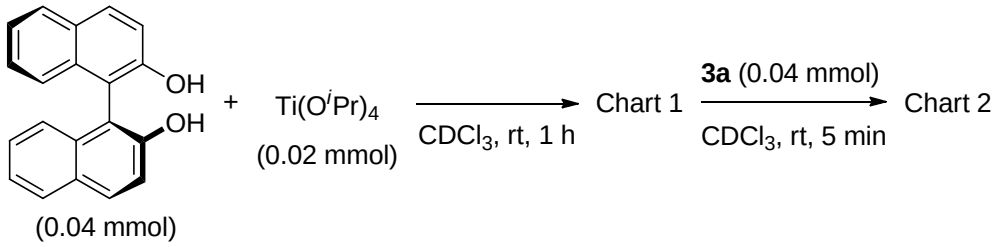
empirical formula	$C_{22}H_{18}ClNO$
formula weight	347.84
crystal system	orthorhombic
space group	$P2_12_12_1$ (#19)
a, Å	10.3718(3)
b, Å	10.7057(3)
c, Å	15.7045(4)
V , Å^3	1743.79(8)
Z	4
D_{calc}, g/cm^3	1.325
T, °C	-150
μ (CuKα), cm^{-1}	19.977
no. of reflns meased	17707
no. of reflns obsd	3158
no. of reflns variable	226
R (All reflections)	0.0379
R_w (All reflections)	0.0829
Goodness of Fit	1.087
Max Shift/Error	0.001
Flack Parameter (Friedel pairs = 1331)	-0.027(12)

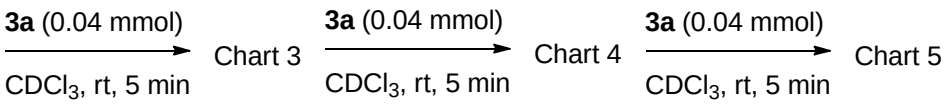
The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 861535). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.

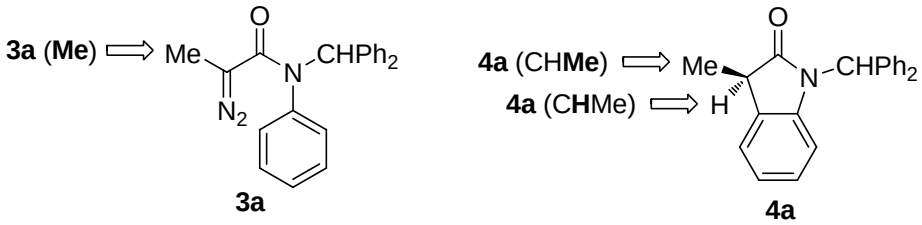

O2
N3
Cl1

^{1}H NMR study of the catalyst solution

To a solution of (*S*)-BINOL (0.04 mmol, 11.4 mg) in $CDCl_3$ (0.60 mL) were added $Ti(O^iPr)_4$ (0.02 mmol, 5.9 μL) at room temperature. After 1 h, the catalyst solution was subjected to ^{1}H NMR analysis (Chart 1). To this catalyst solution was then added an aliquot of diazoamide **3a** (0.04 mmol, 13.7 mg) at room temperature and immediately taken to ^{1}H NMR analysis (Chart 2). This procedure was repeated 4 times till the consumption of **3a** become apparently sluggish (Charts 3-5). For comparison, ^{1}H NMR spectra of (*S*)-BINOL (Chart 6), $Ti(O^iPr)_4$ (Chart 7), and a 1:1 mixture of $Ti(O^iPr)_4$ and (*S*)-BINOL (Chart 8) in $CDCl_3$ were also attached.







Charts 1-5.

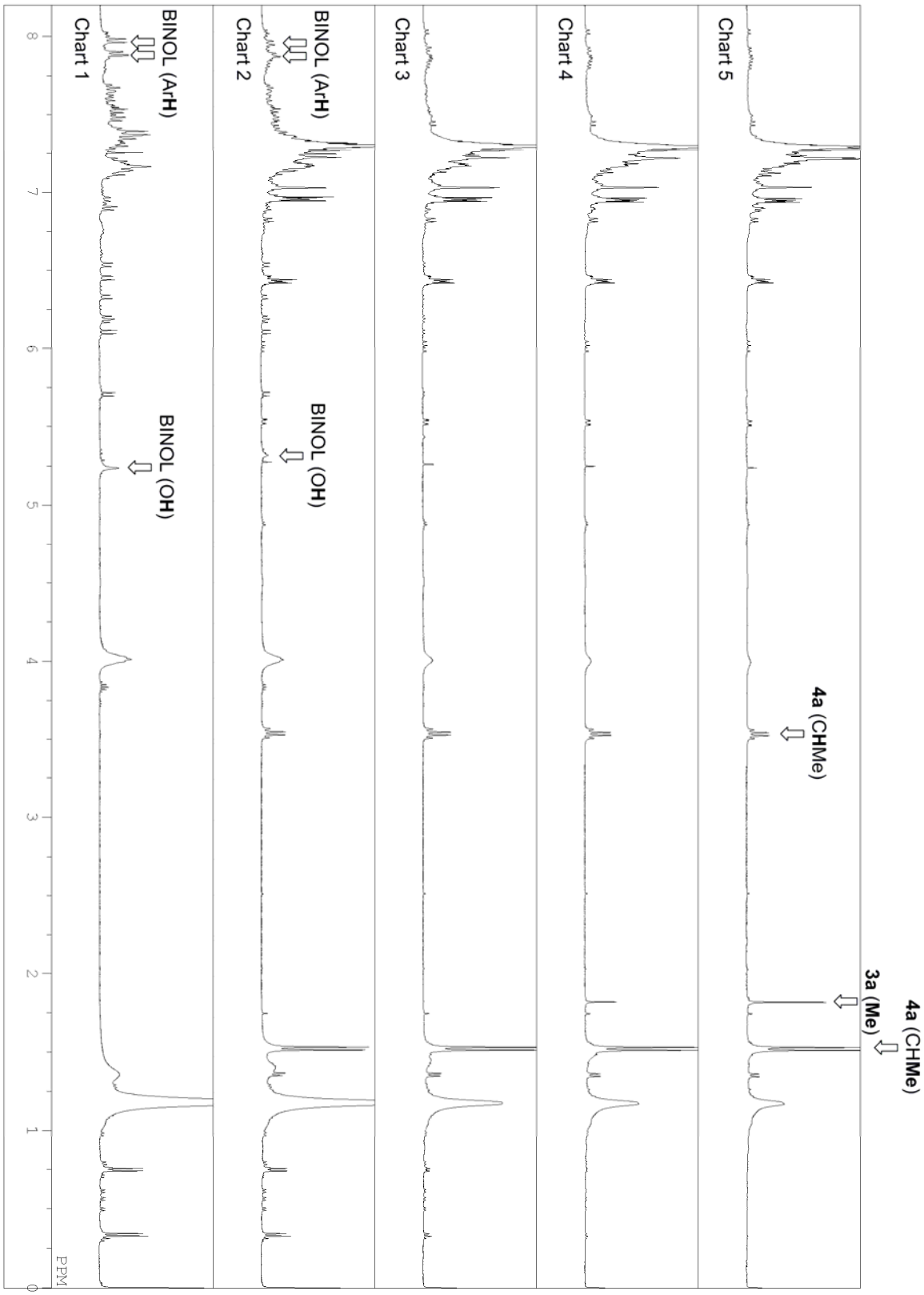

4a (CHMe)
3a (Me)
Chart 5
4a (CHMe)
Chart 4
Chart 3
BINOL (ArH)
BINOL (OH)
Chart 2
BINOL (ArH)
BINOL (OH)
Chart 1
PPM

Chart 6. (*S*)-BINOL

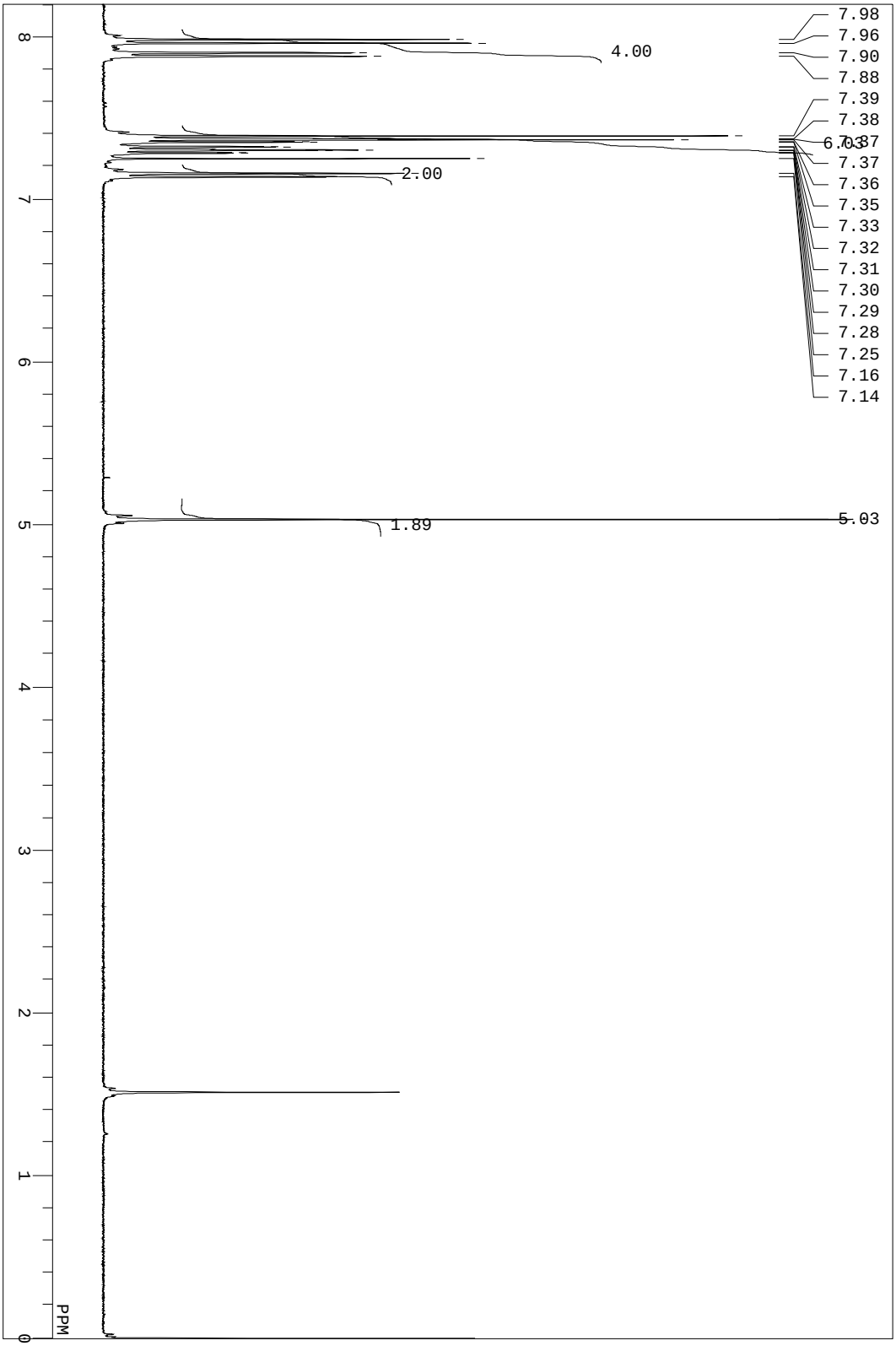


Chart 7. $Ti(O^iPr)_4$

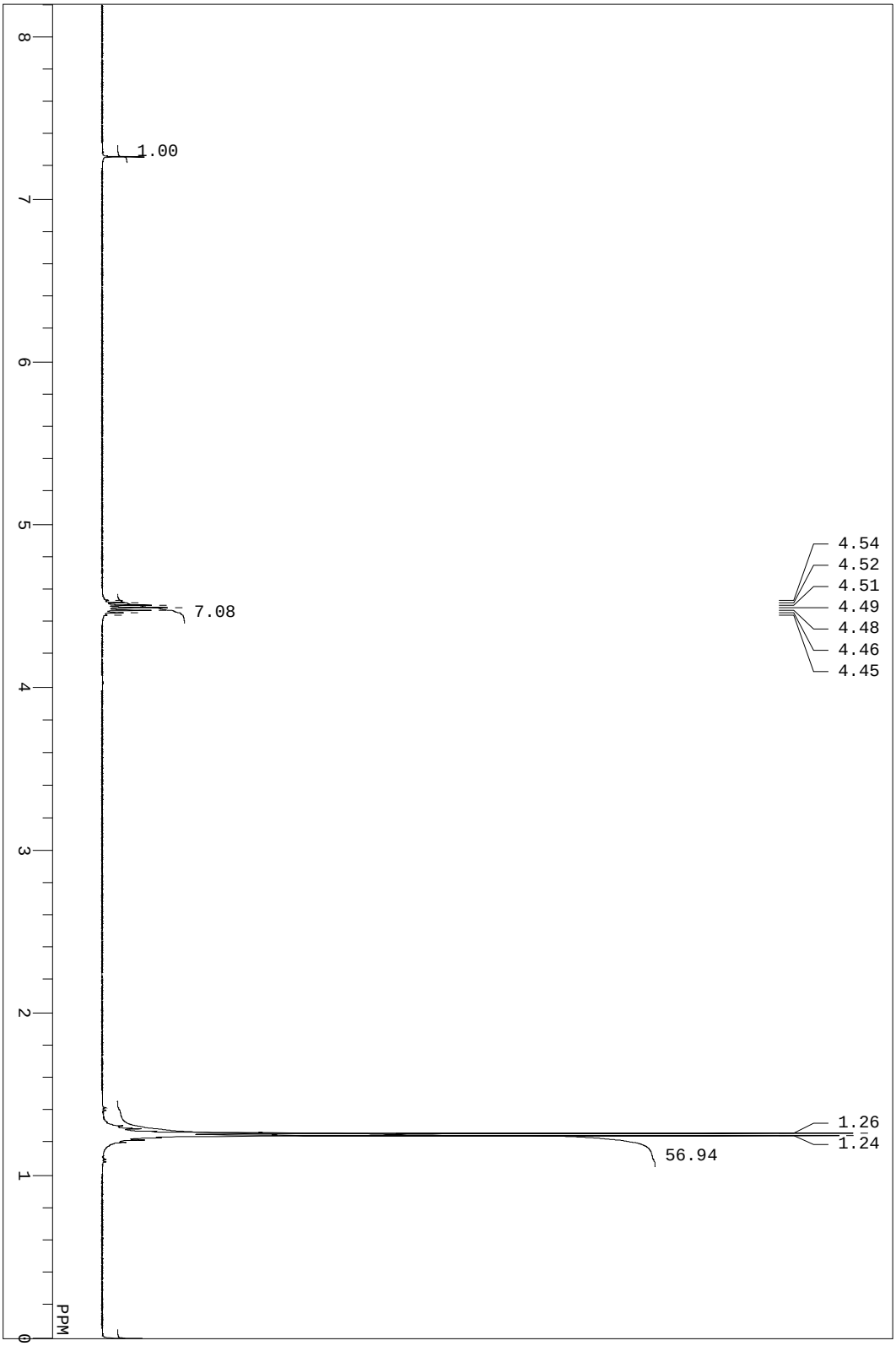
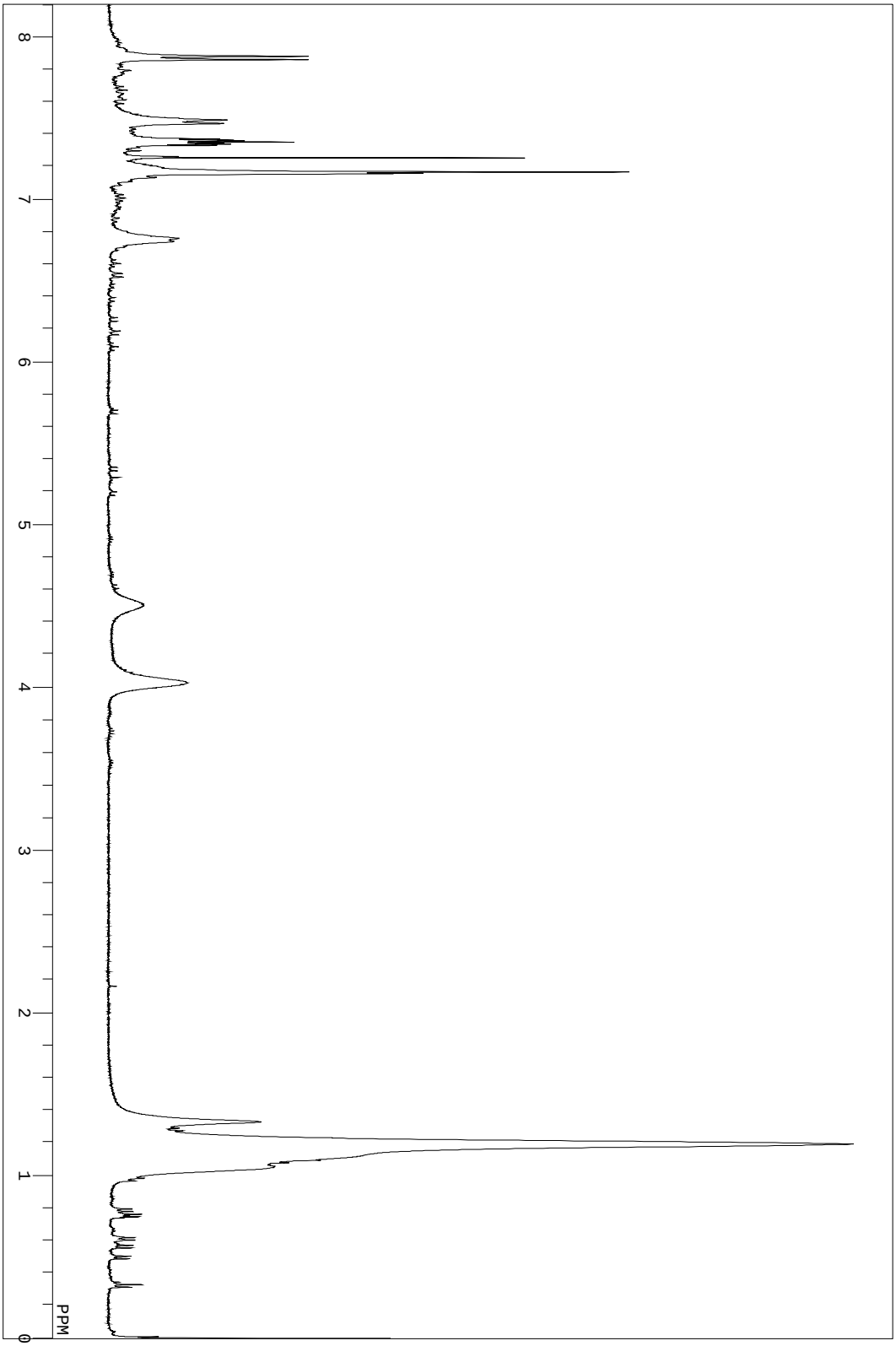


Chart 8. A 1:1 mixture of $Ti(O^iPr)_4$ and (*S*)-BINOL

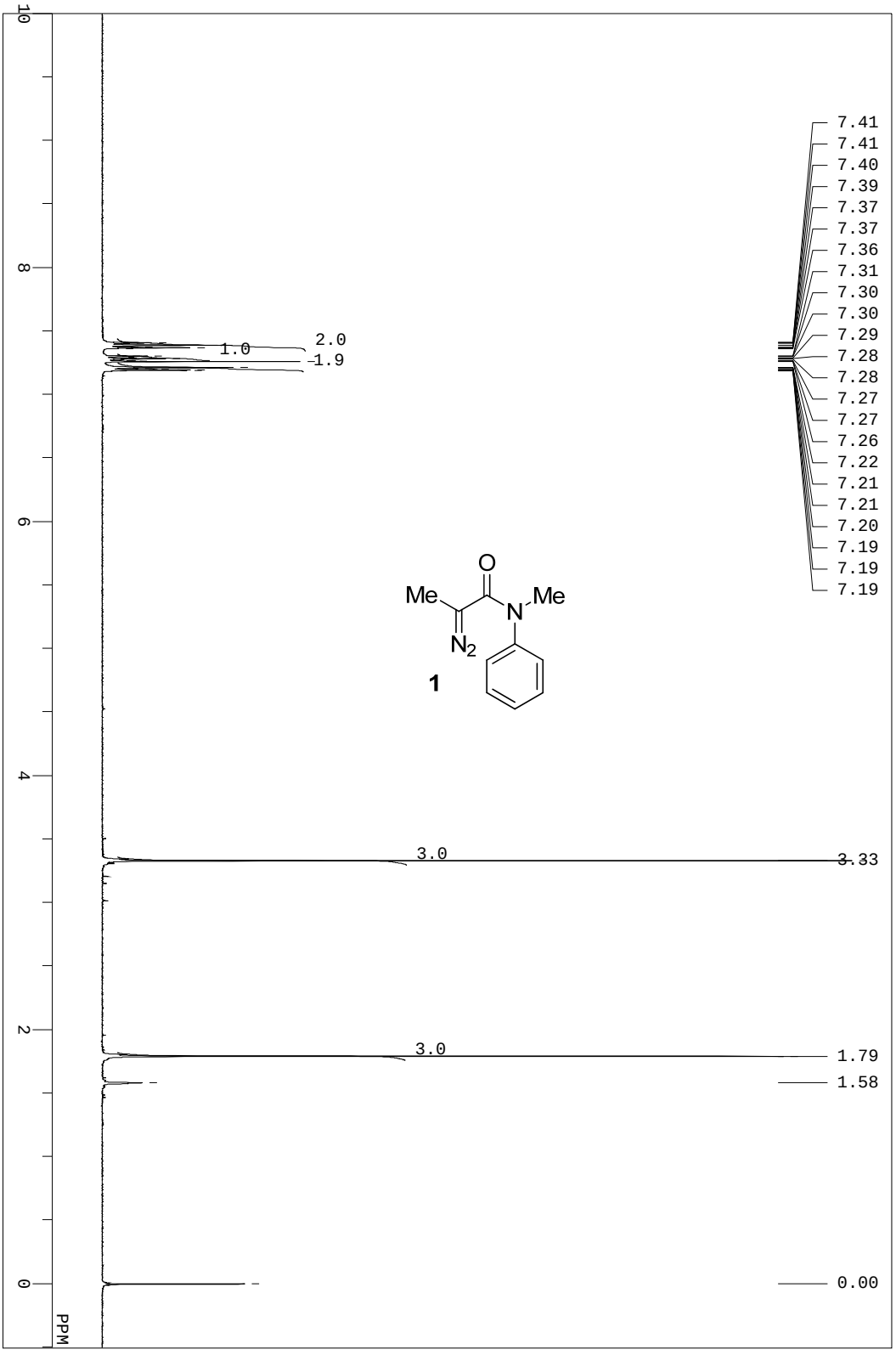


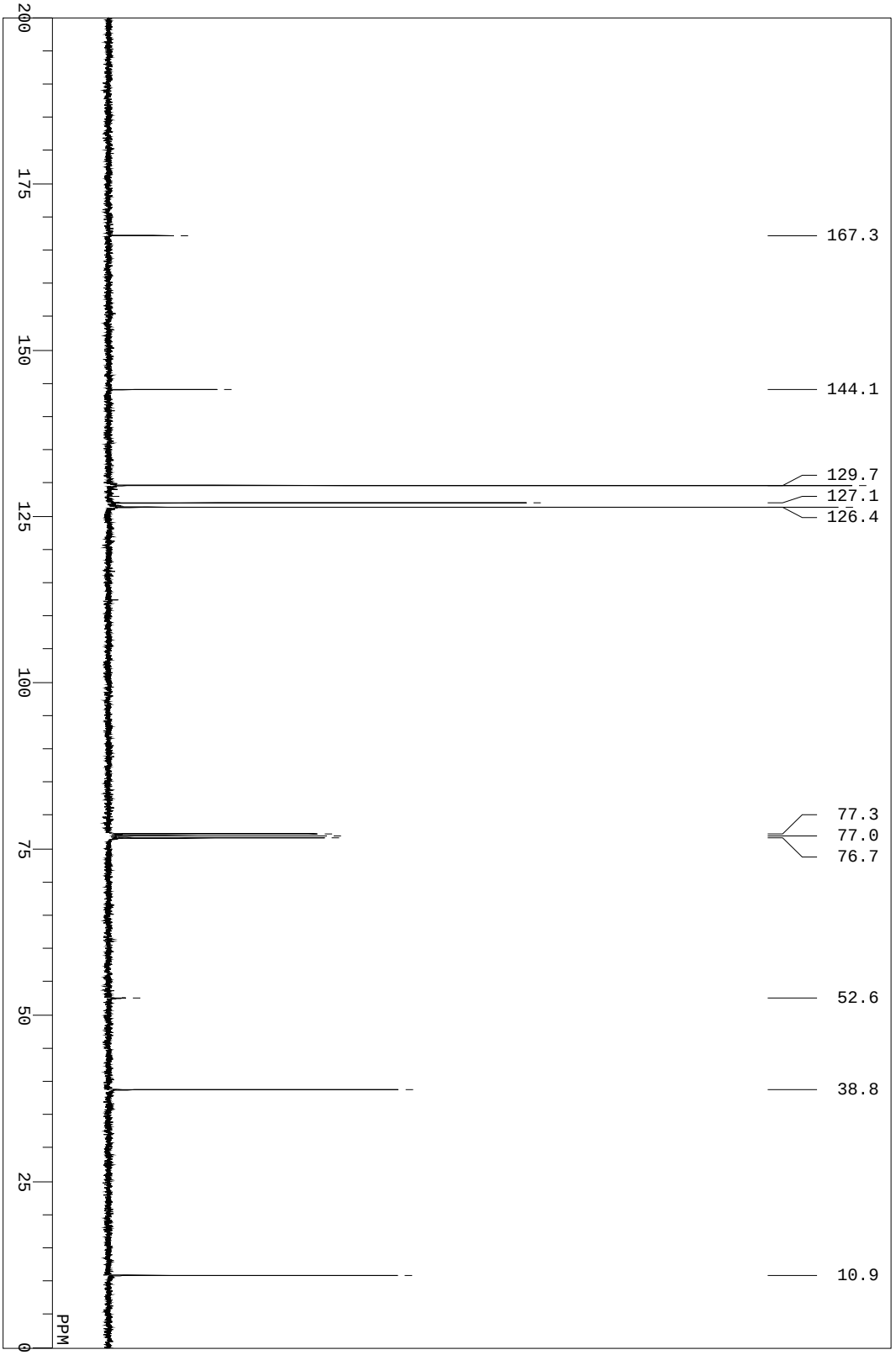
References

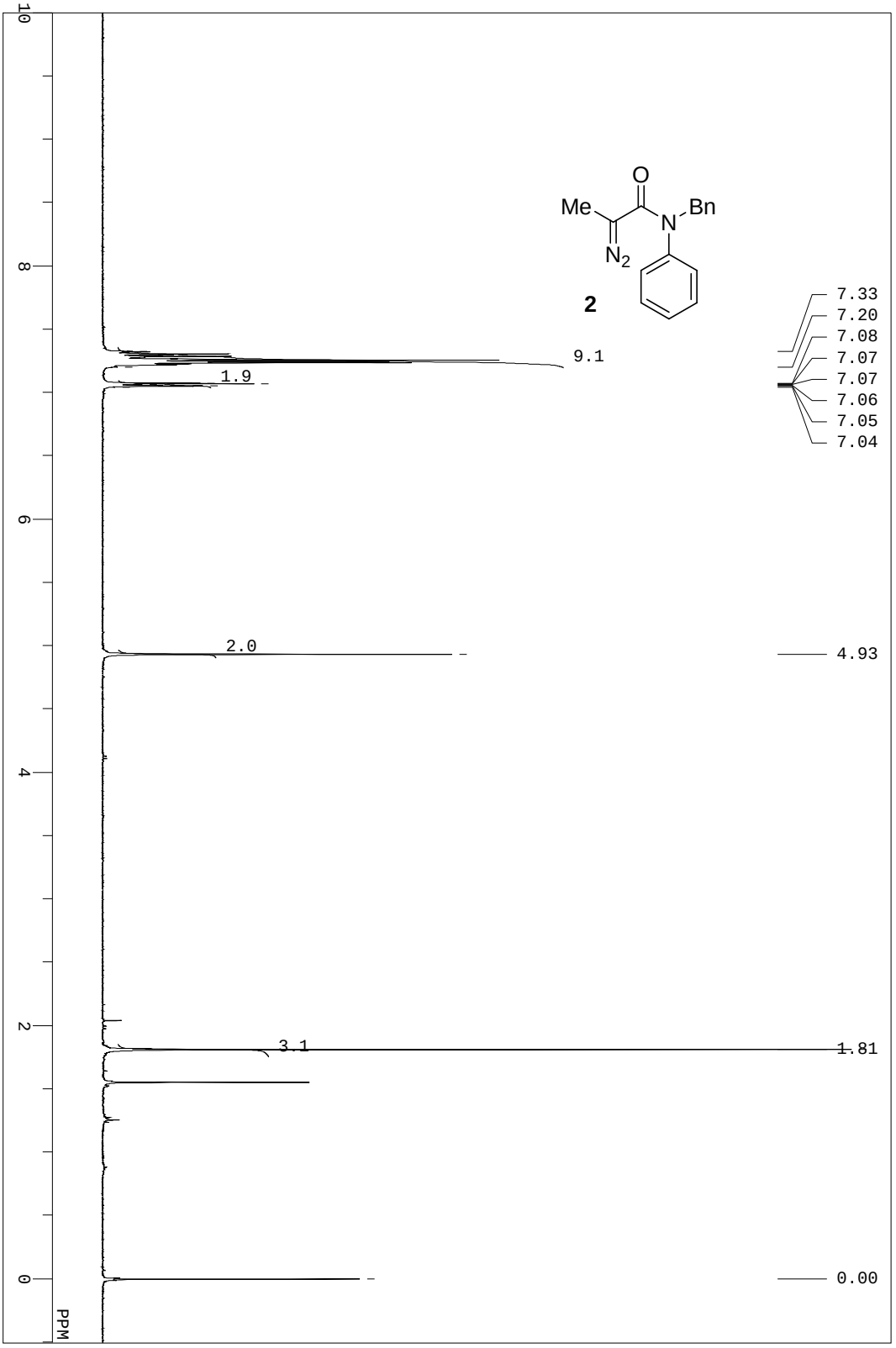
(1) Rahman, O.; Kihlberg, T.; Långström, B. *Org. Biomol. Chem.* **2004**, *2*, 1612.

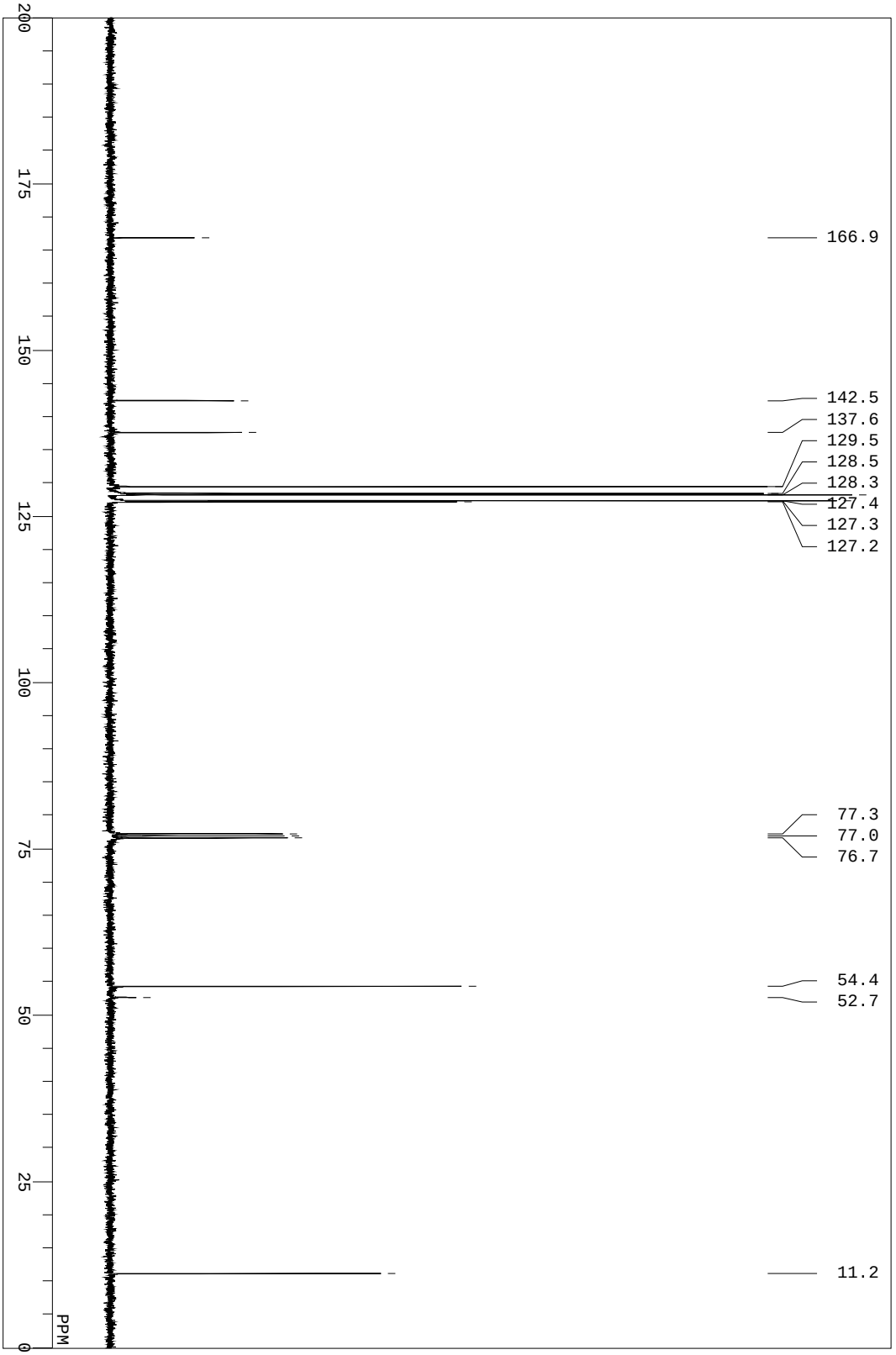
(2) We observed substantial loss of the enantioselectivity (at most 8-10% ee in case of the products with electron-withdrawing groups like **4c** and **4d**, when the column chromatography was conducted without dry ice jacket.

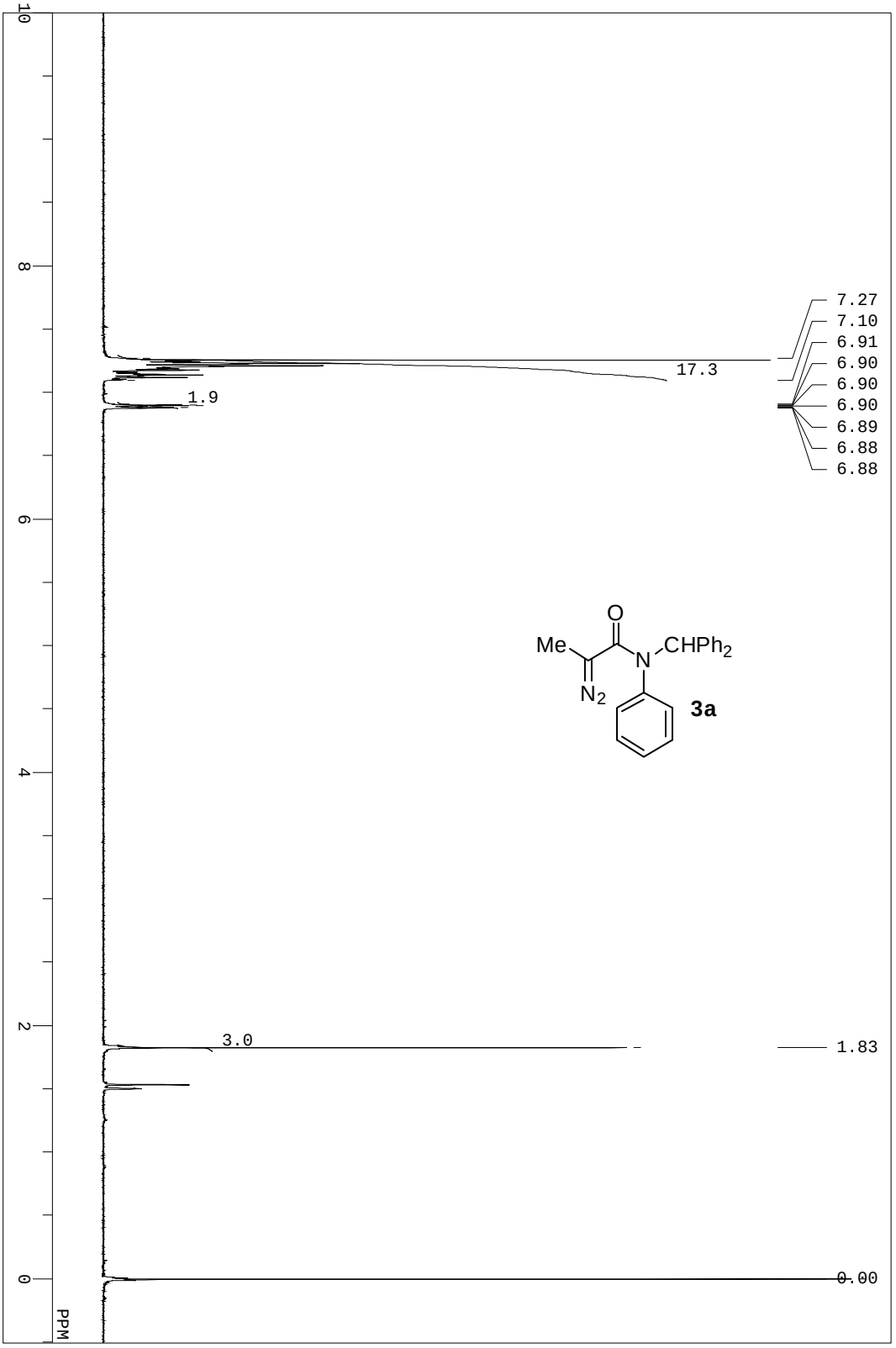
(3) Sheldrick, G.M. *Acta Cryst.* **2008**, A64, 112.

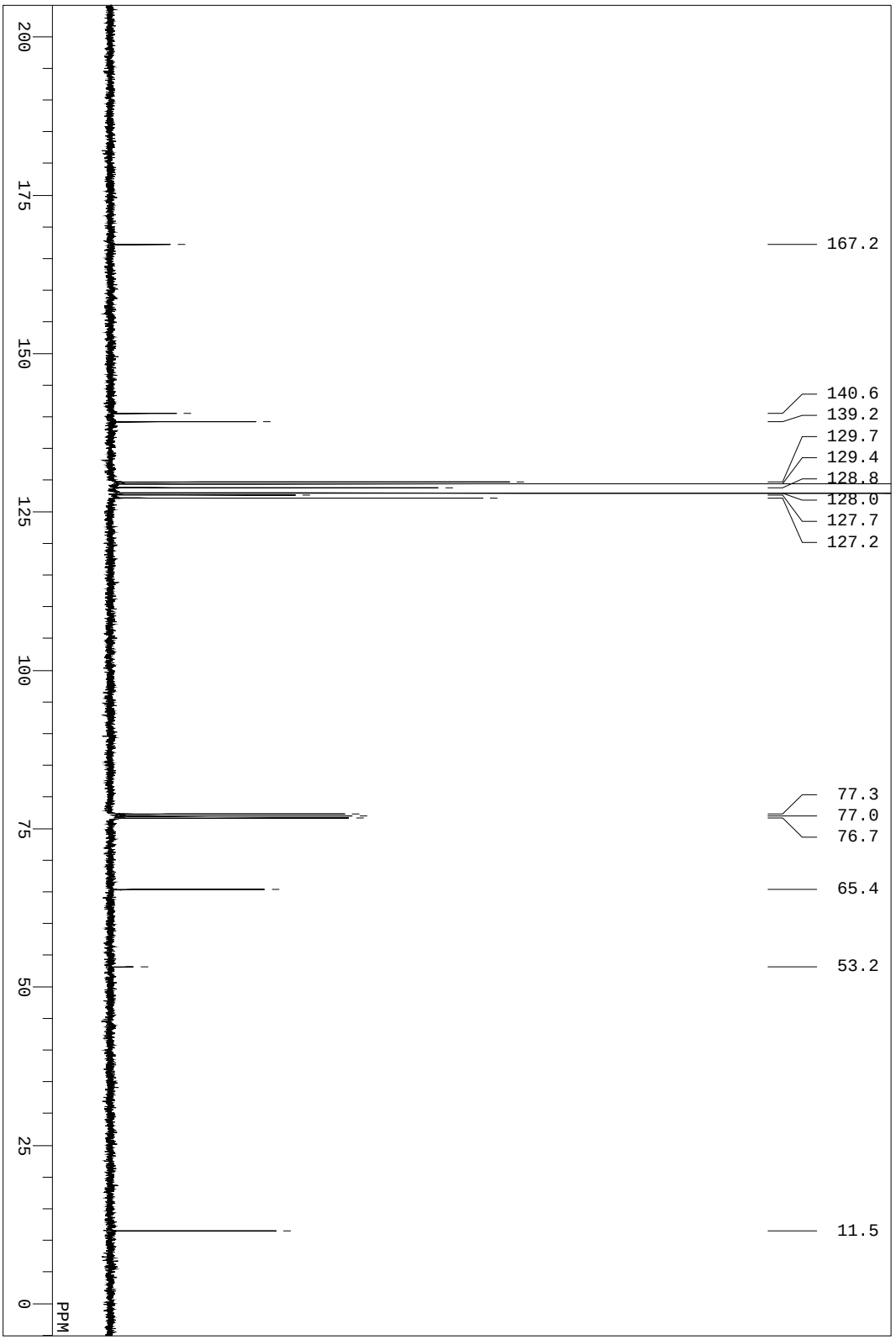

10
8
6
4
2
0
PPM
7.41
7.41
7.40
7.39
7.37
7.37
7.36
7.31
7.30
7.30
7.29
7.28
7.28
7.27
7.27
7.26
7.22
7.21
7.21
7.20
7.19
7.19
7.19
2.0
1.0
1.9
3.0
3.33
3.0
1.79
1.58
0.00
Me
O
N
Me
N2
1

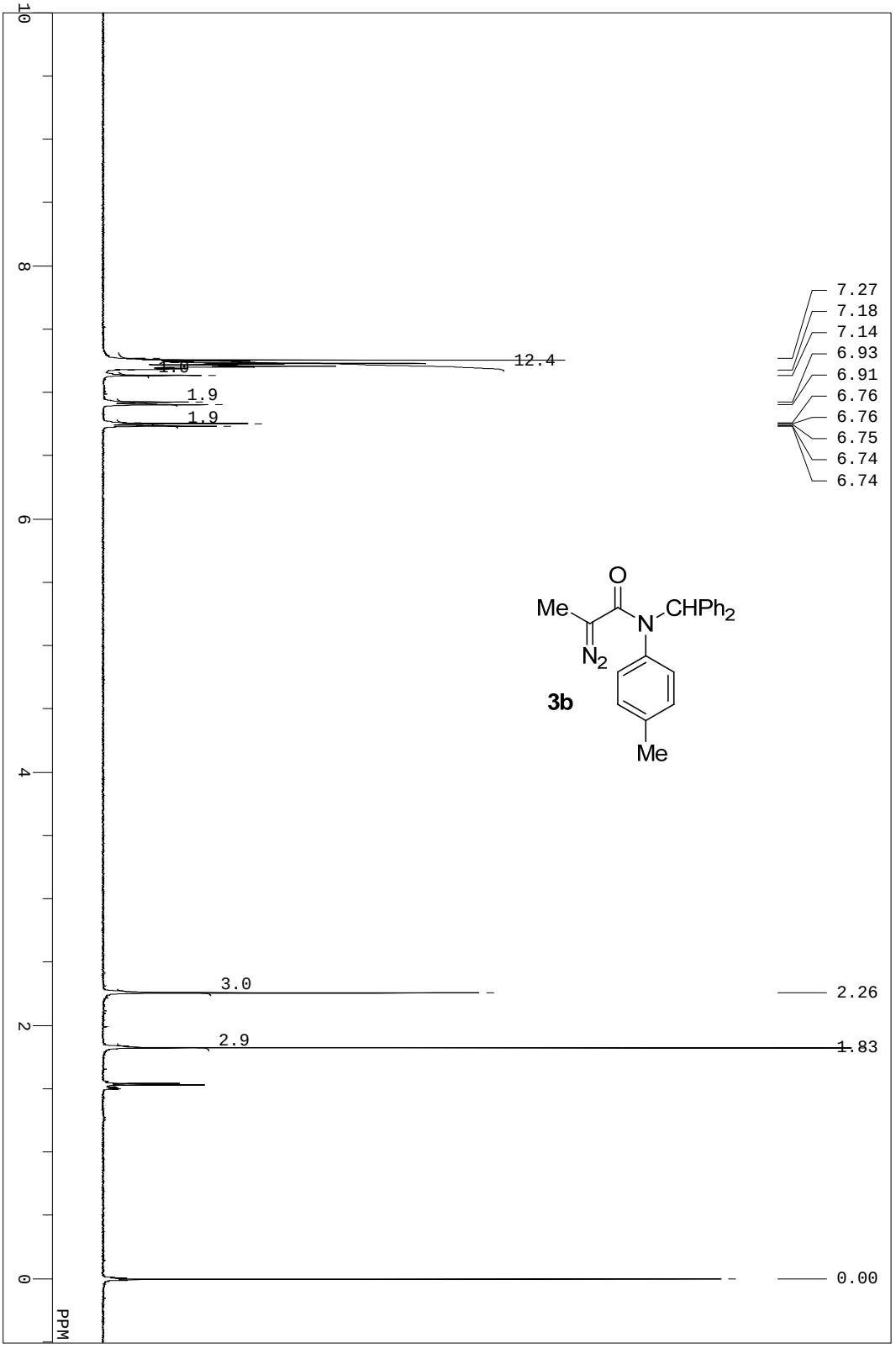

200
175
150
125
100
75
50
25
0
PPM
167.3
144.1
129.7
127.1
126.4
77.3
77.0
76.7
52.6
38.8
10.9

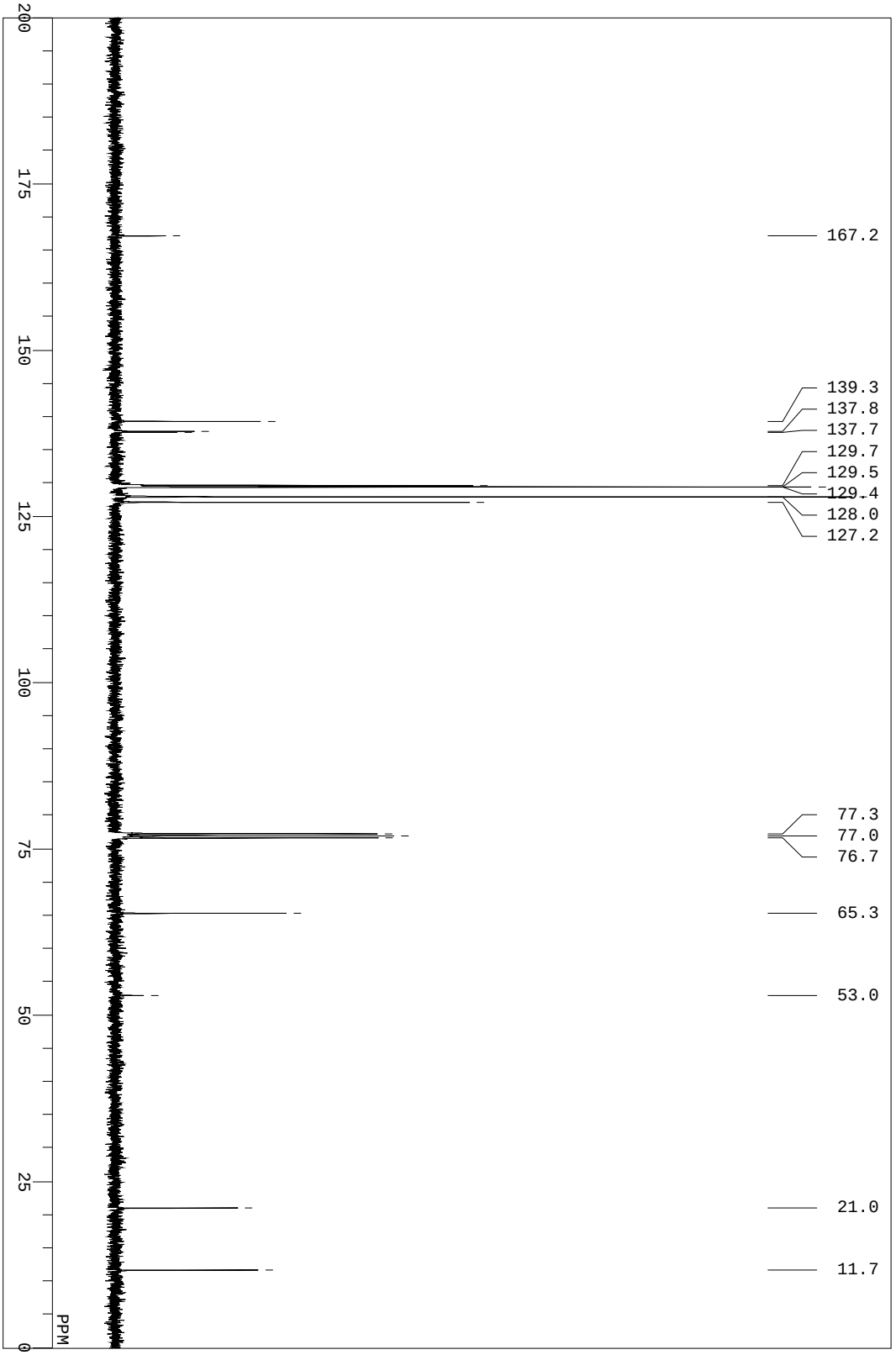

10
8
6
4
2
0
PPM
O
Me
N
Bn
N2
2
9.1
1.9
2.0
3.1
7.33
7.20
7.08
7.07
7.07
7.06
7.05
7.04
4.93
1.81
0.00

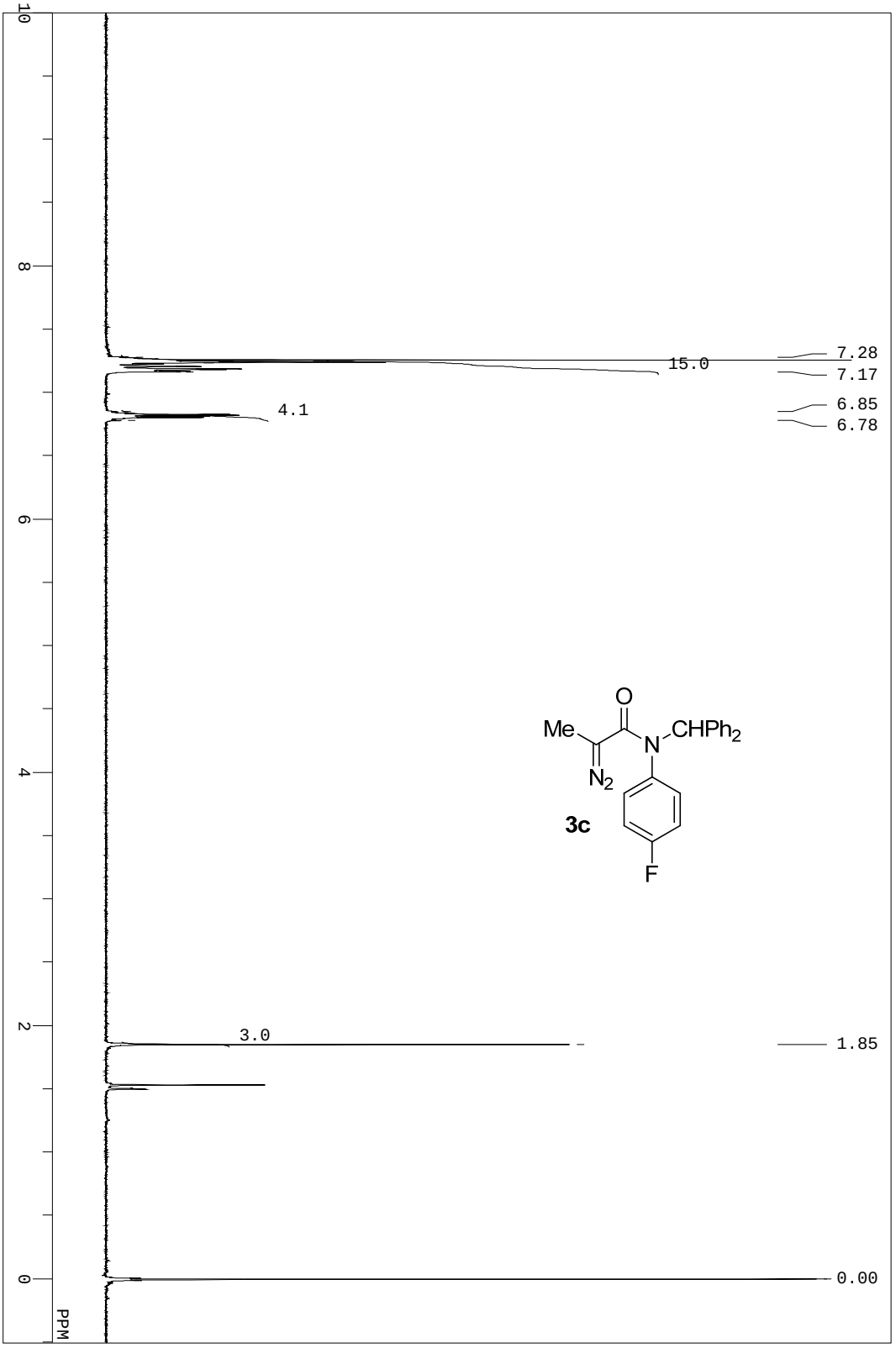

200
175
150
125
100
75
50
25
0
PPM
166.9
142.5
137.6
129.5
128.5
128.3
127.4
127.3
127.2
77.3
77.0
76.7
54.4
52.7
11.2

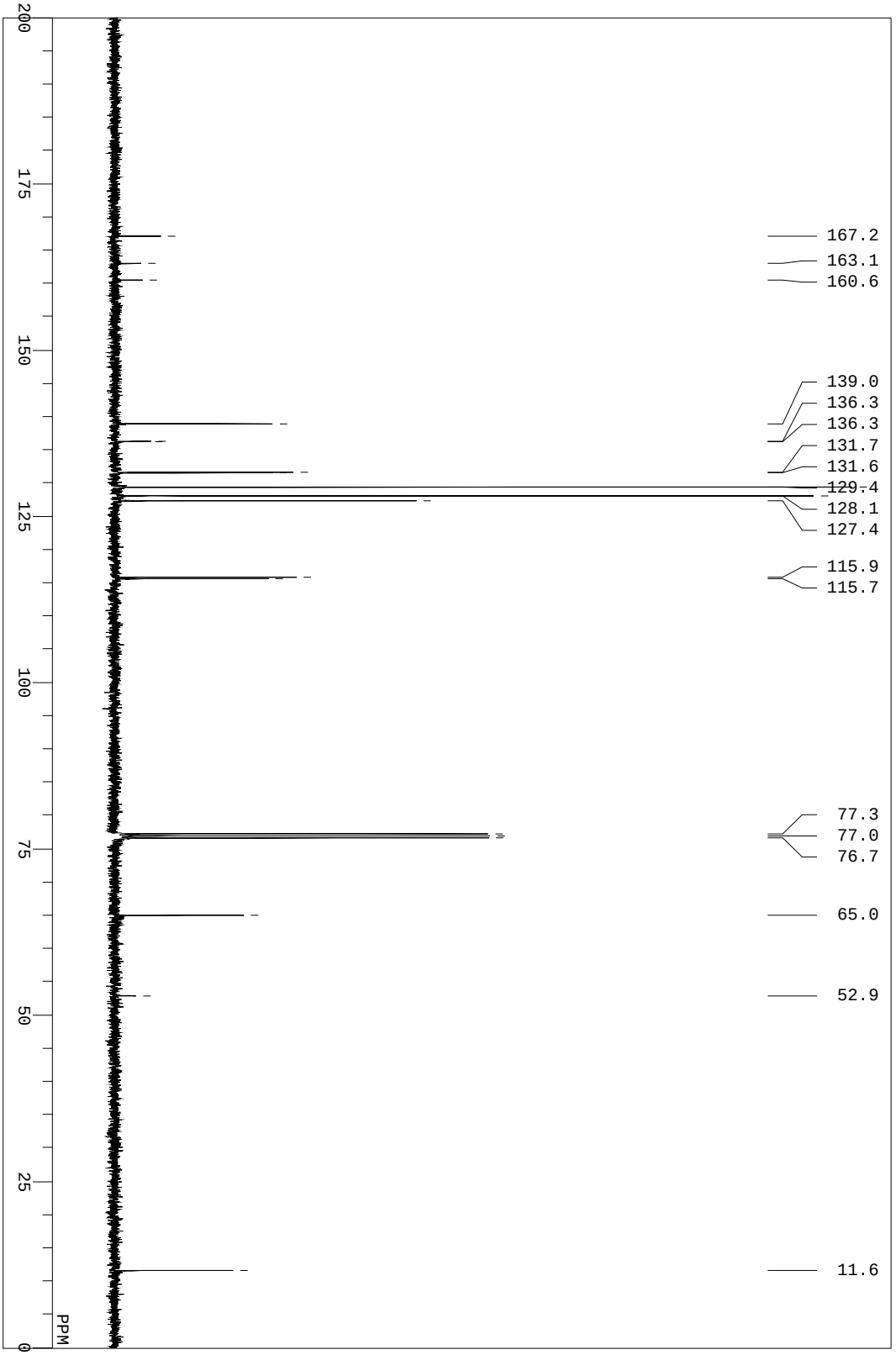

10
8
6
4
2
0
PPM
7.27
7.10
6.91
6.90
6.90
6.90
6.89
6.88
6.88
17.3
1.9
3.0
1.83
0.00
O
Me
N
CHPh2
N2
3a

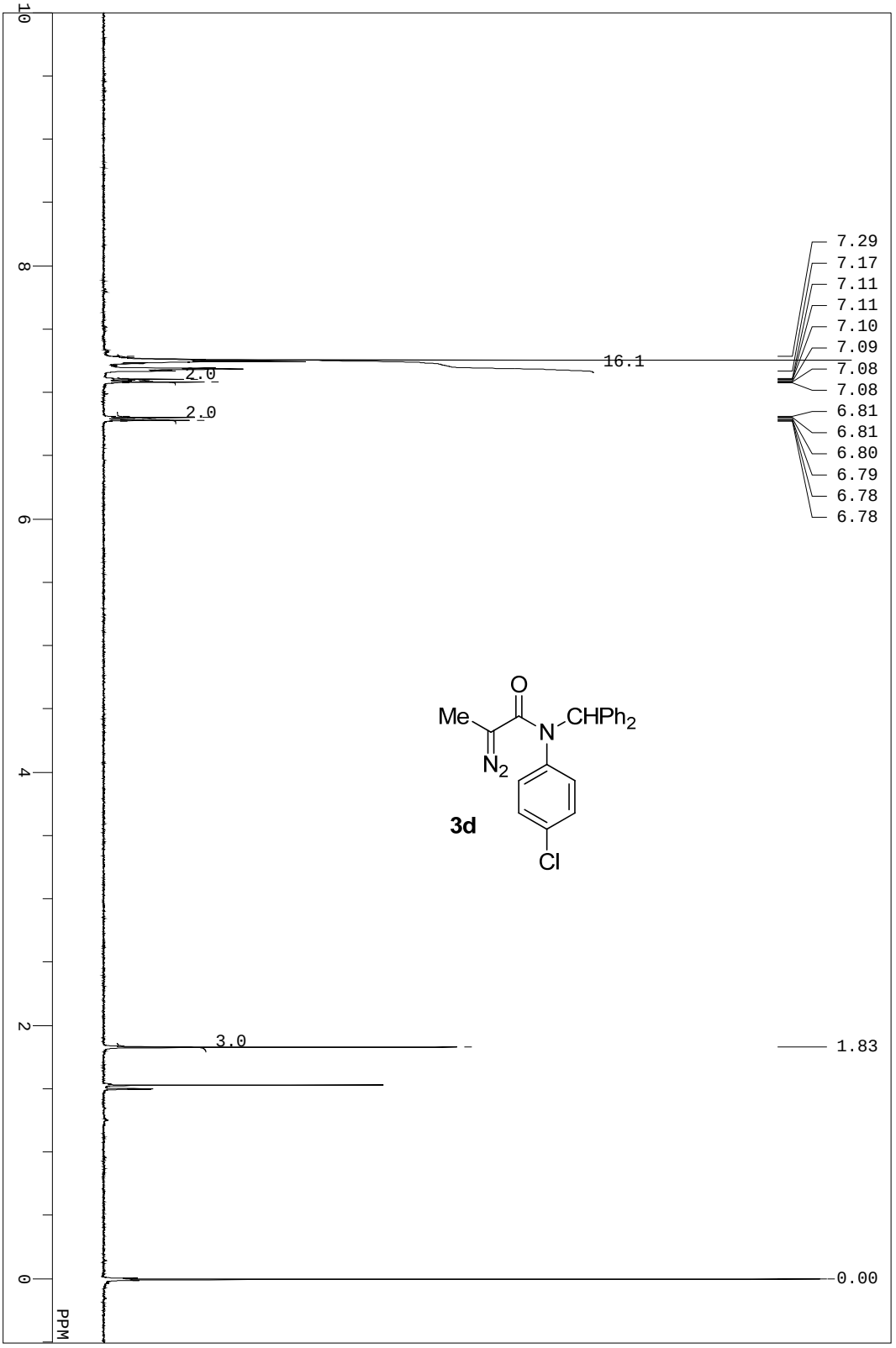

200
175
150
125
100
75
50
25
0
PPM
167.2
140.6
139.2
129.7
129.4
128.8
128.0
127.7
127.2
77.3
77.0
76.7
65.4
53.2
11.5

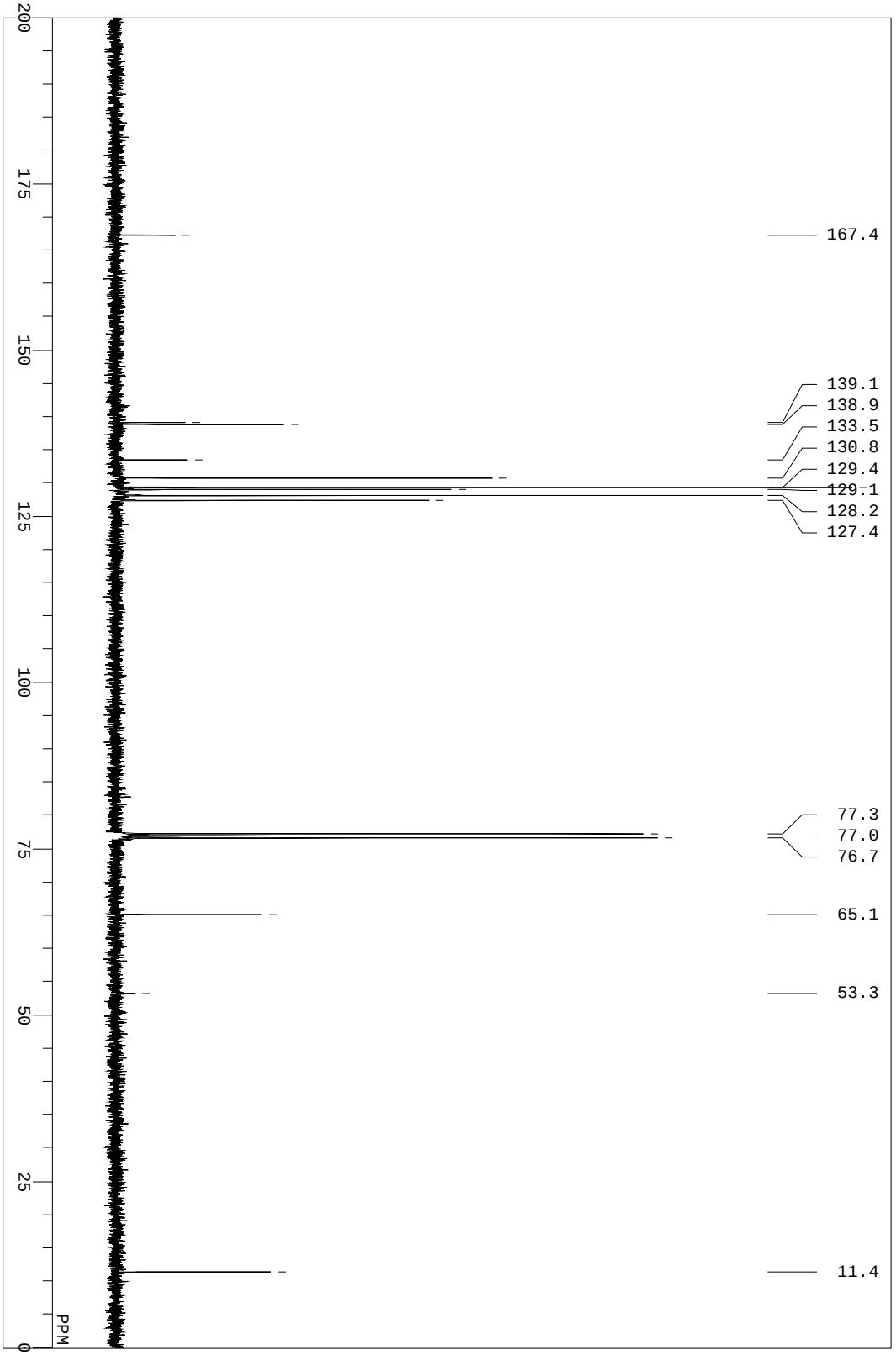

10
8
6
4
2
0
PPM
12.4
1.0
1.9
1.9
3.0
2.9
7.27
7.18
7.14
6.93
6.91
6.76
6.76
6.75
6.74
6.74
2.26
1.83
0.00
O
Me
N
CHPh2
N2
Me
3b

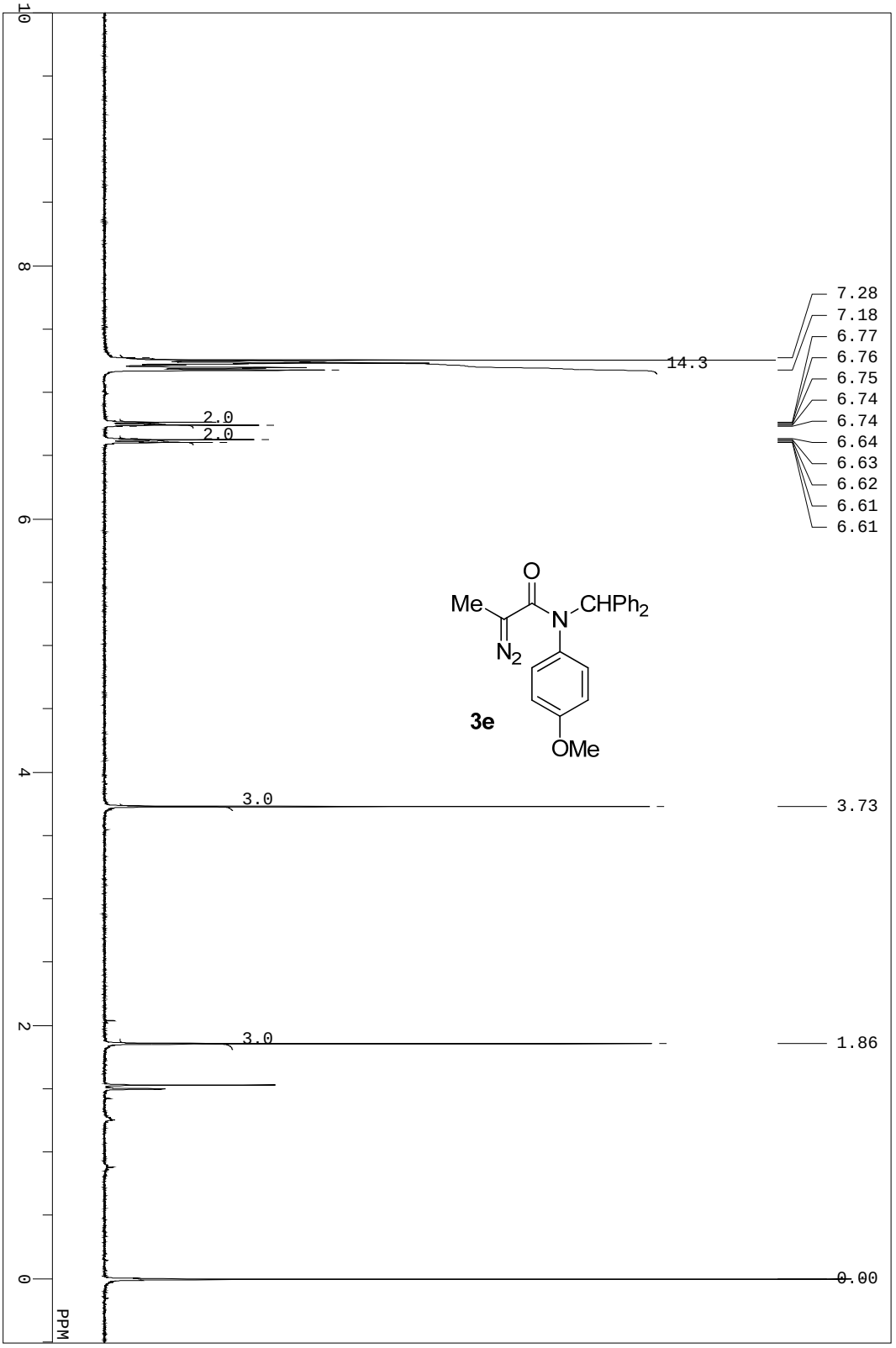

200
175
150
125
100
75
50
25
0
PPM
167.2
139.3
137.8
137.7
129.7
129.5
129.4
128.0
127.2
77.3
77.0
76.7
65.3
53.0
21.0
11.7

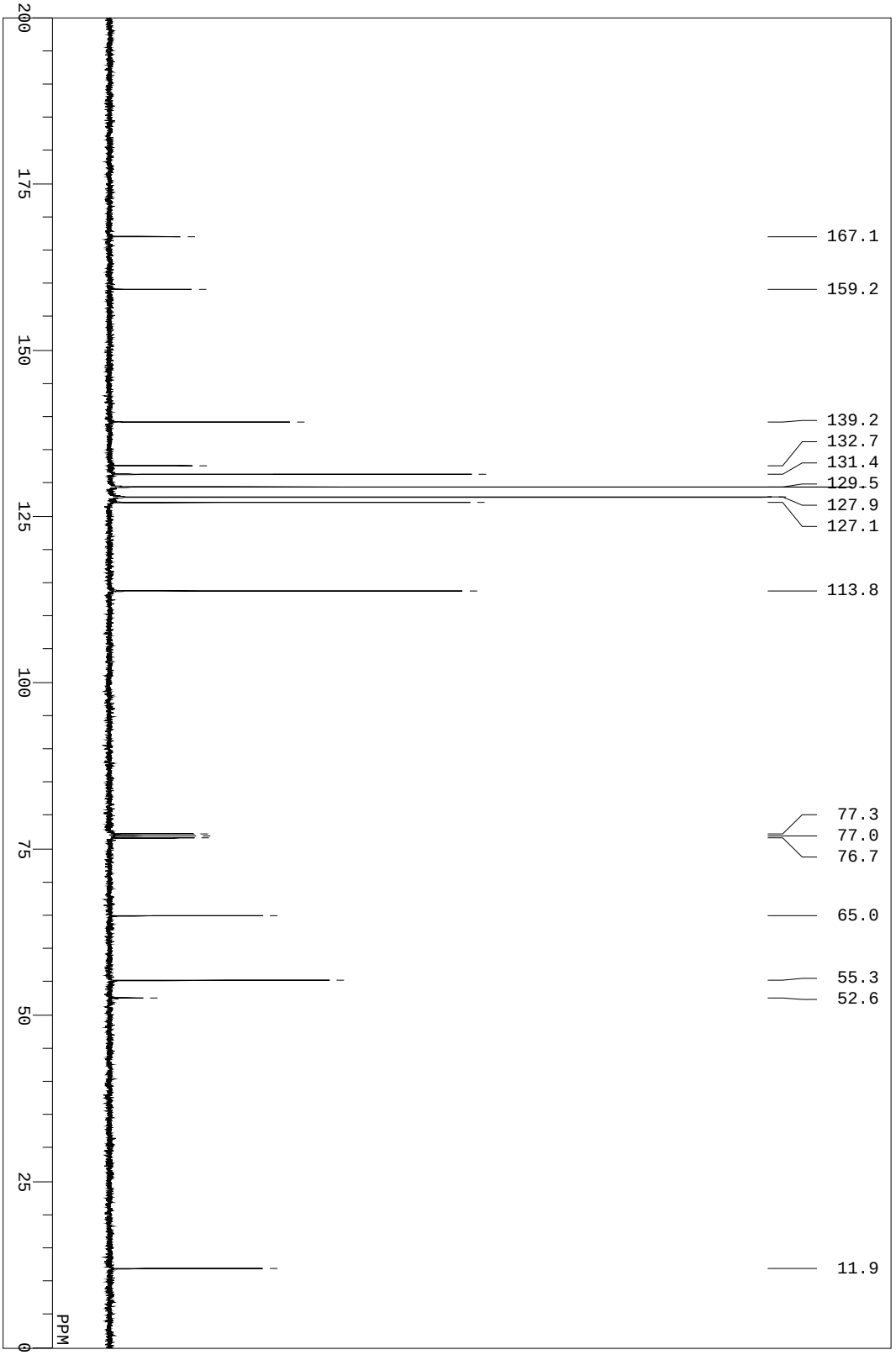

10
8
6
4
2
0
PPM
7.28
7.17
6.85
6.78
1.85
0.00
15.0
4.1
3.0
O
Me
N
CHPh2
N2
F
3c

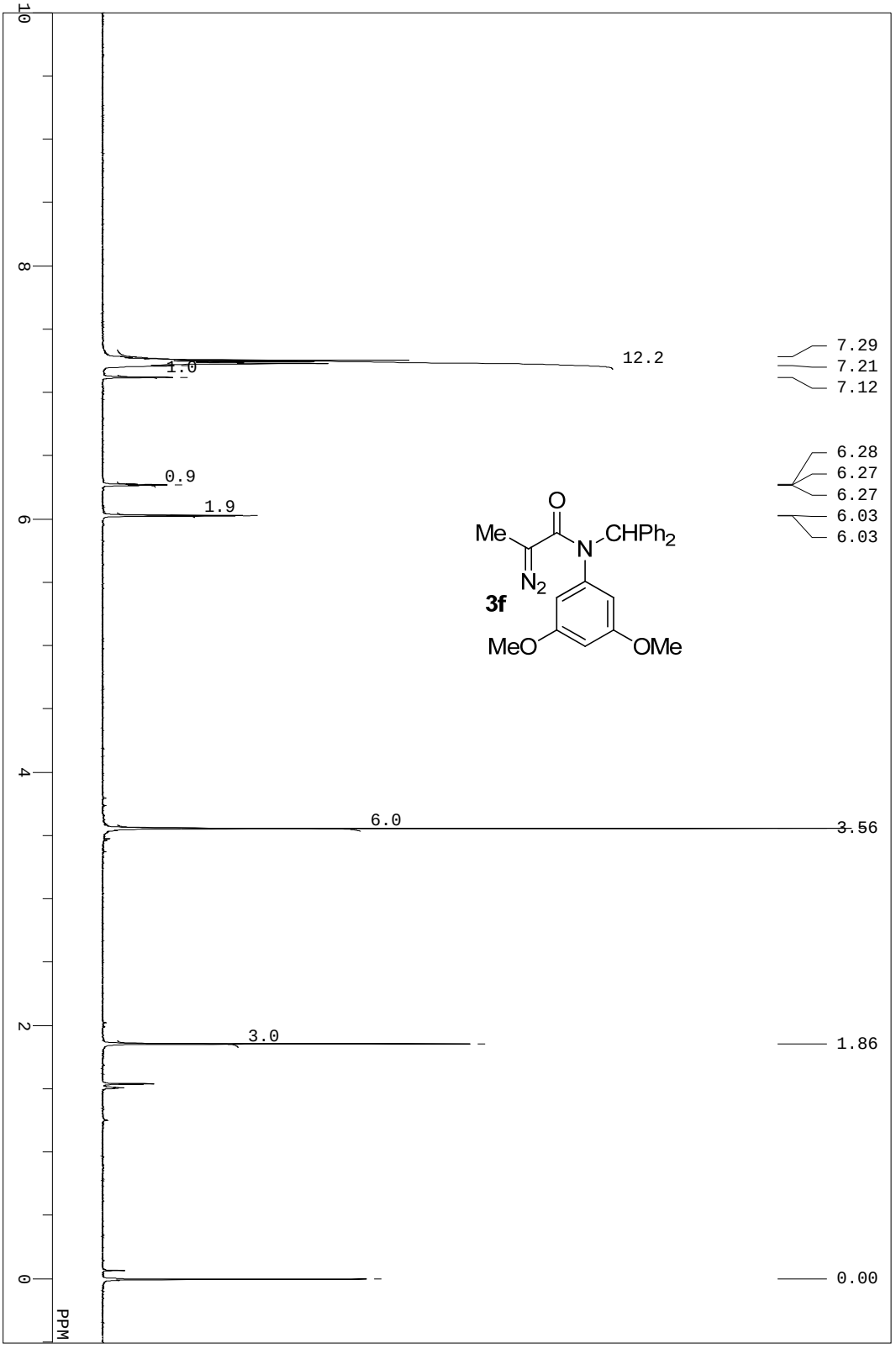

200
175
150
125
100
75
50
25
0
PPM
167.2
163.1
160.6
139.0
136.3
136.3
131.7
131.6
129.4
128.1
127.4
115.9
115.7
77.3
77.0
76.7
65.0
52.9
11.6

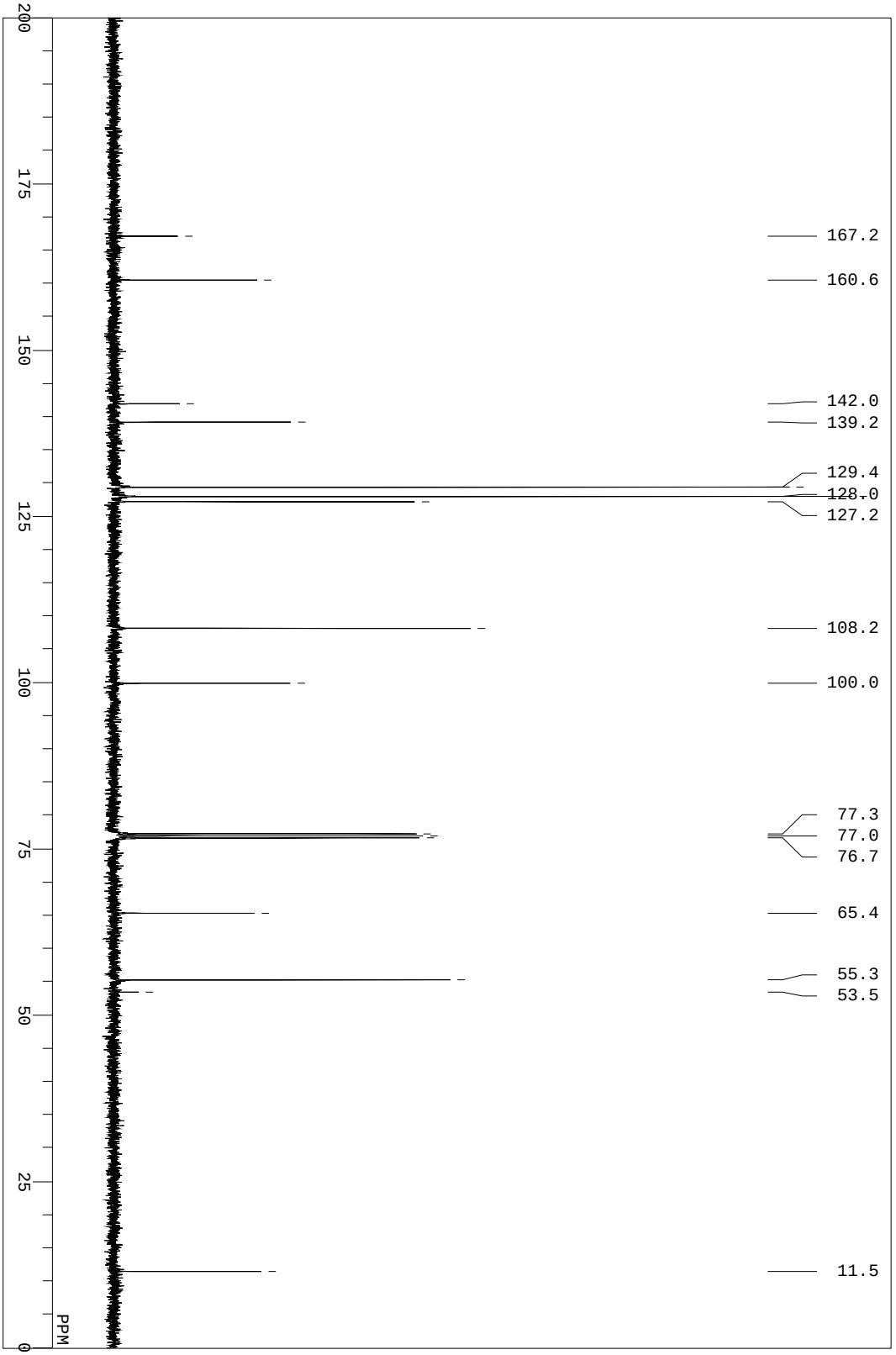

7.29
7.17
7.11
7.11
7.10
7.09
7.08
7.08
6.81
6.81
6.80
6.79
6.78
6.78
16.1
2.0
2.0
3.0
1.83
0.00
PPM
Me
O
N
CHPh2
N2
Cl
3d

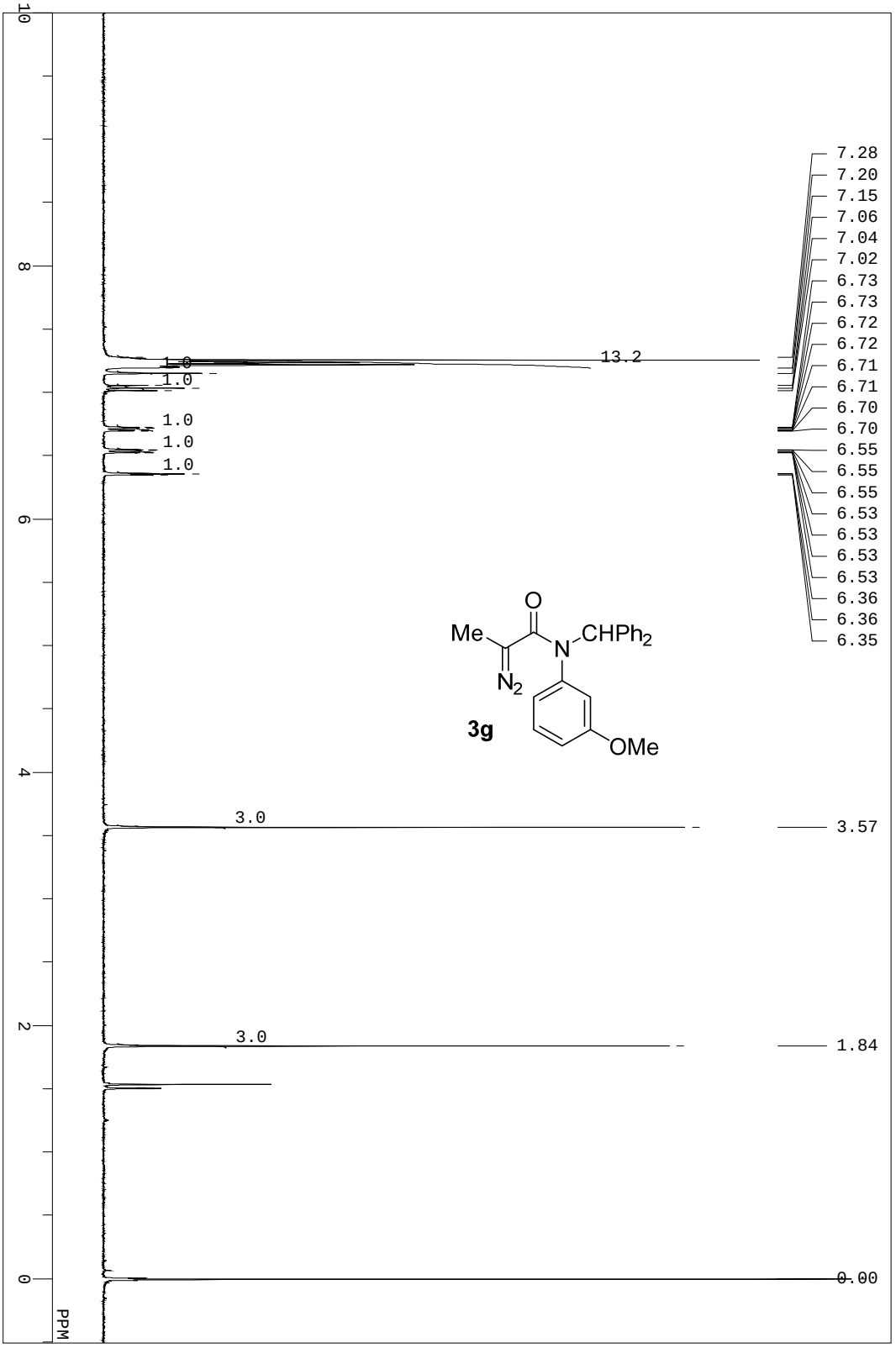

200
175
150
125
100
75
50
25
0
PPM
167.4
139.1
138.9
133.5
130.8
129.4
129.1
128.2
127.4
77.3
77.0
76.7
65.1
53.3
11.4

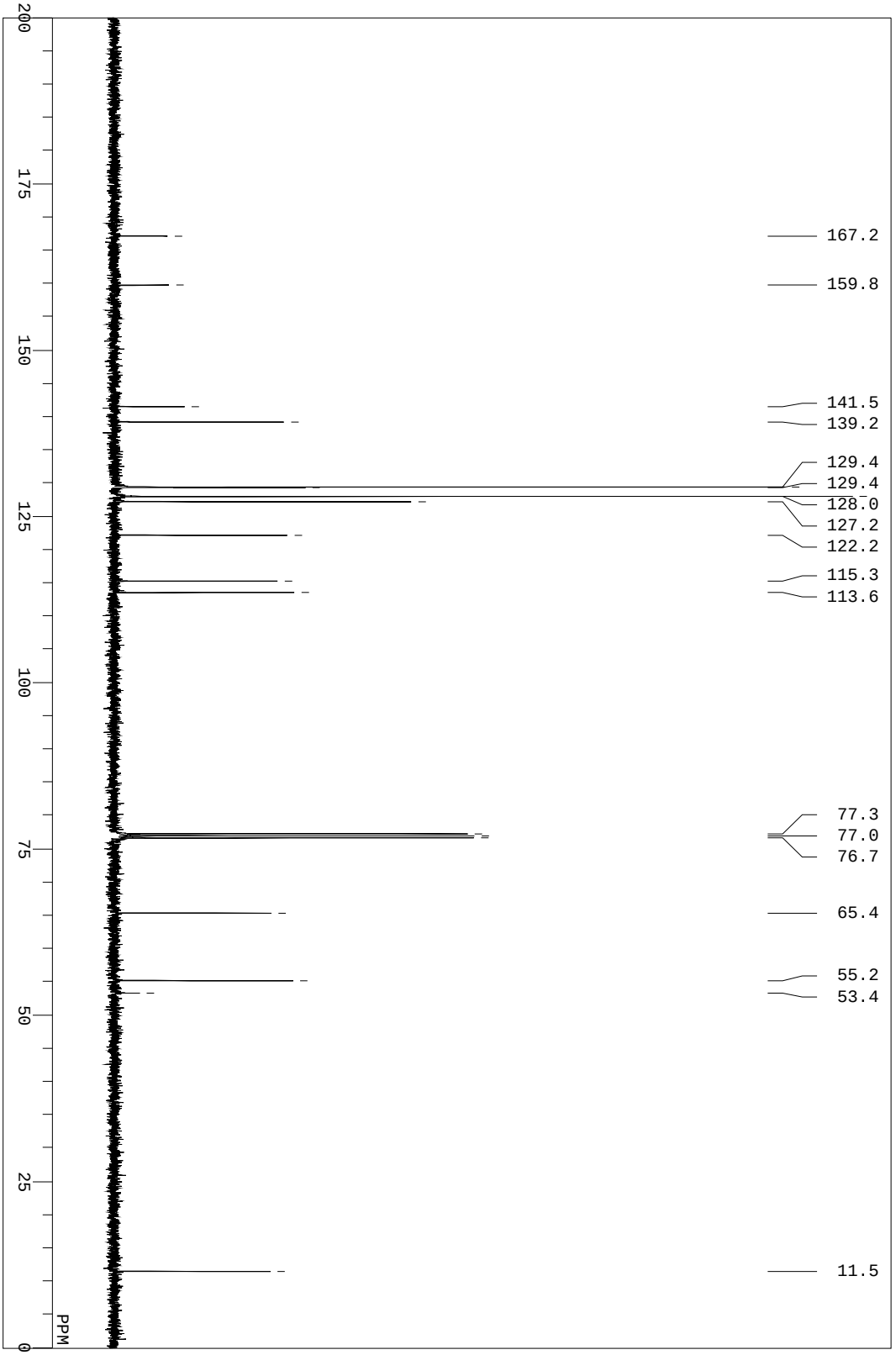

10
8
6
4
2
0
PPM
7.28
7.18
6.77
6.76
6.75
6.74
6.74
6.64
6.63
6.62
6.61
6.61
14.3
2.0
2.0
3.0
3.73
3.0
1.86
0.00
O
Me
CHPh2
N
N2
OMe
3e

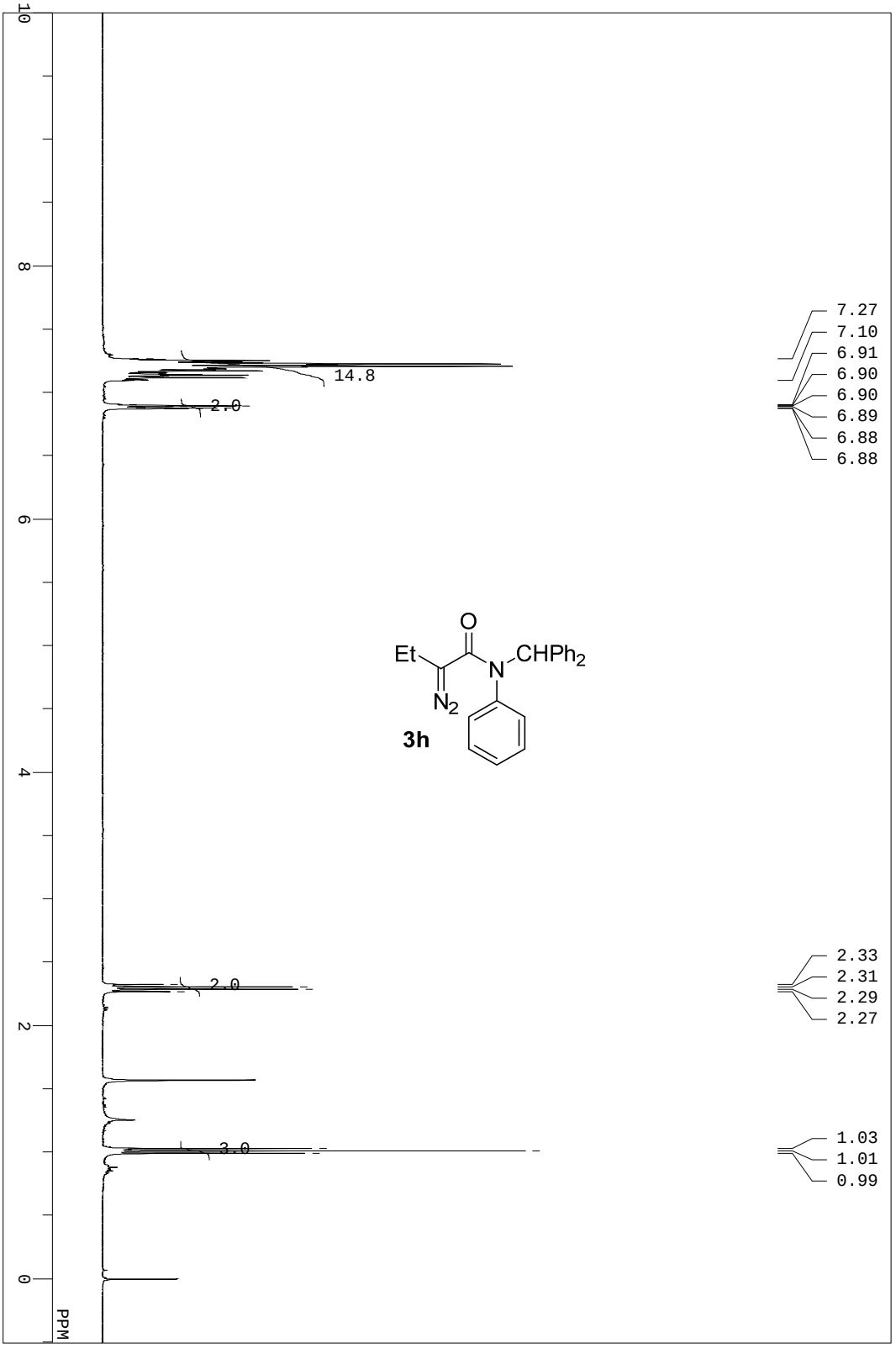

200
175
150
125
100
75
50
25
0
PPM
167.1
159.2
139.2
132.7
131.4
129.5
127.9
127.1
113.8
77.3
77.0
76.7
65.0
55.3
52.6
11.9

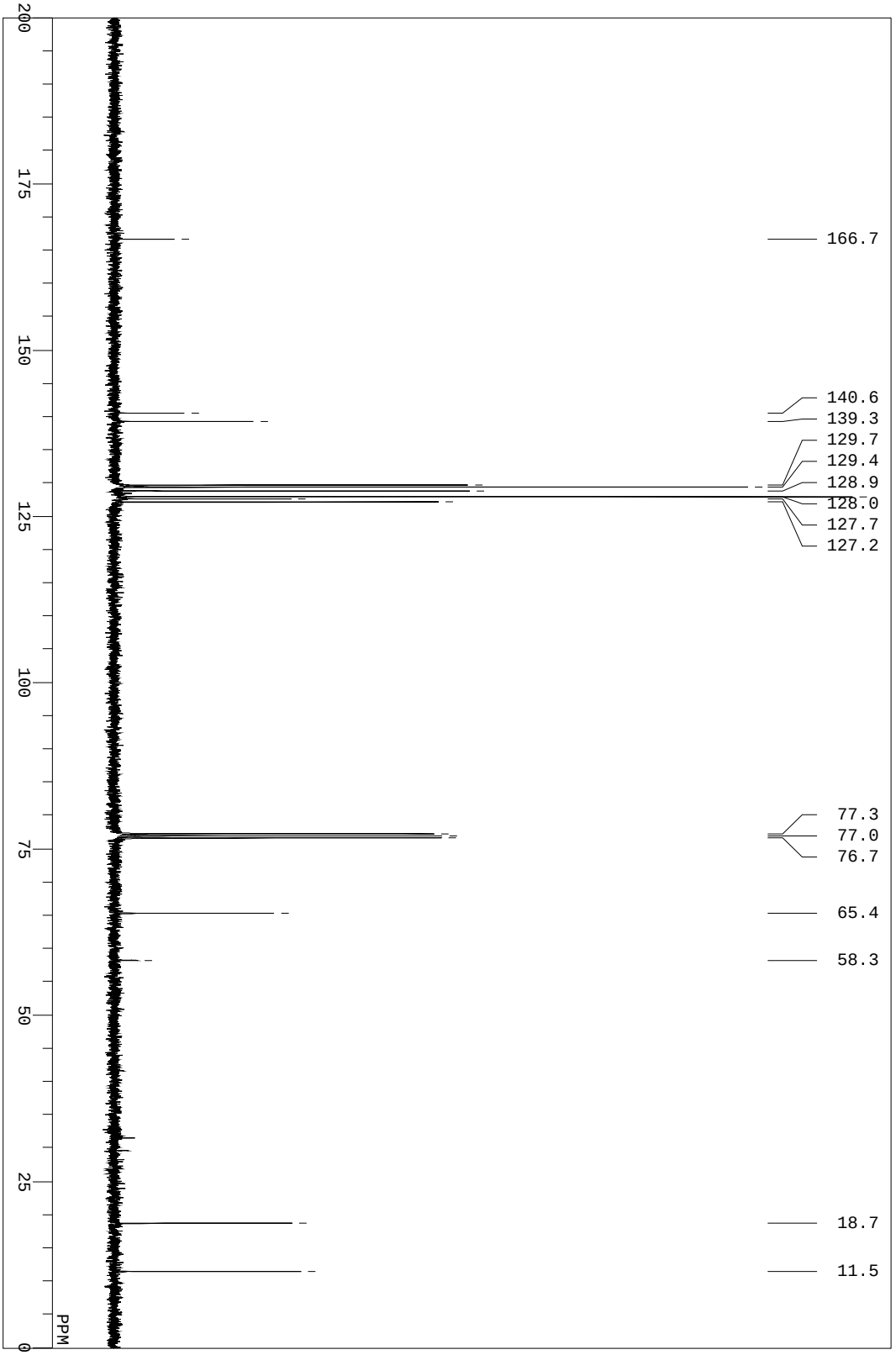

10
8
6
4
2
0
PPM
12.2
1.0
0.9
1.9
6.0
3.0
7.29
7.21
7.12
6.28
6.27
6.27
6.03
6.03
3.56
1.86
0.00
Me
O
N
CHPh2
N2
3f
MeO
OMe

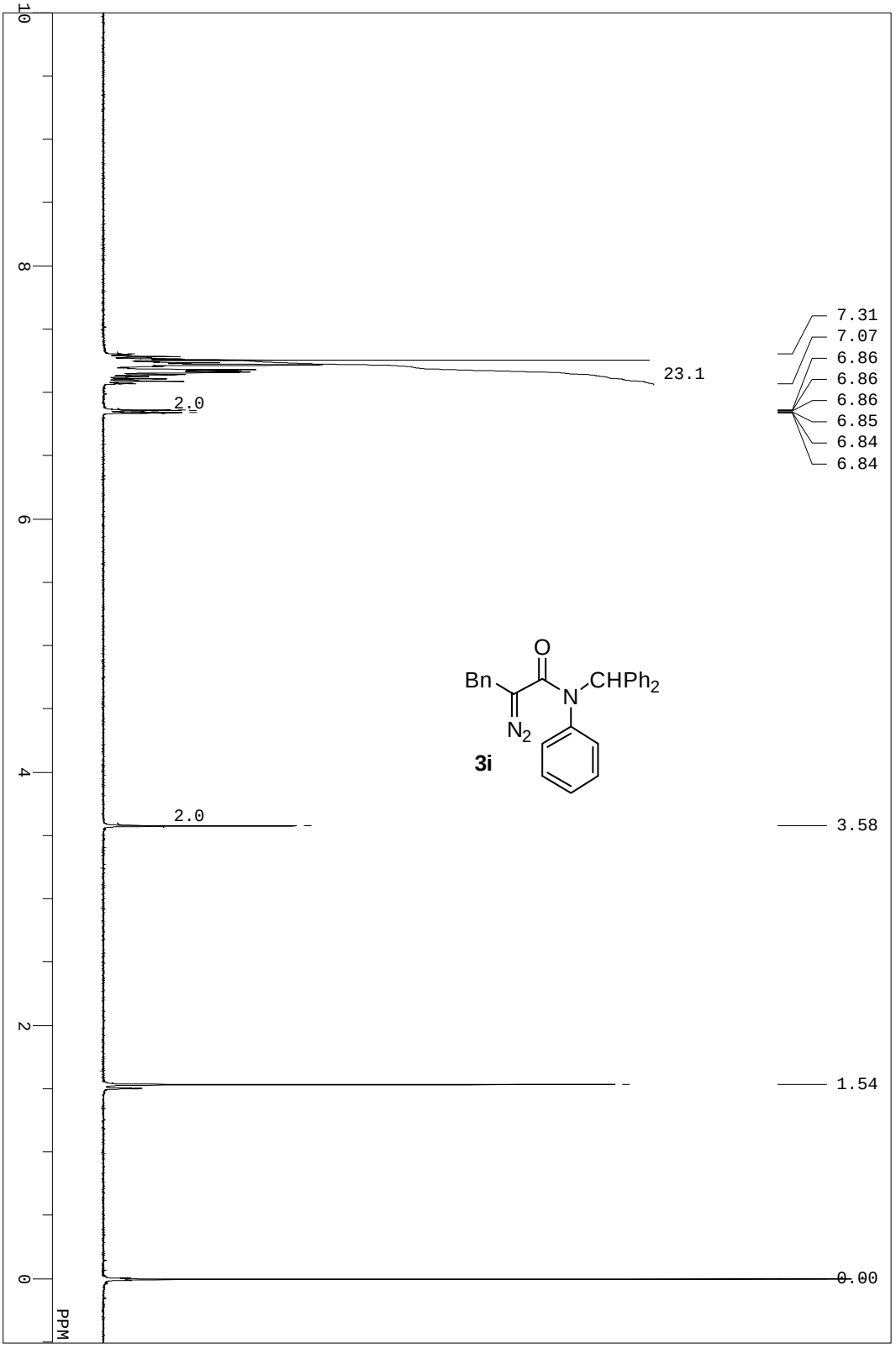

200
175
150
125
100
75
50
25
0
PPM
167.2
160.6
142.0
139.2
129.4
128.0
127.2
108.2
100.0
77.3
77.0
76.7
65.4
55.3
53.5
11.5

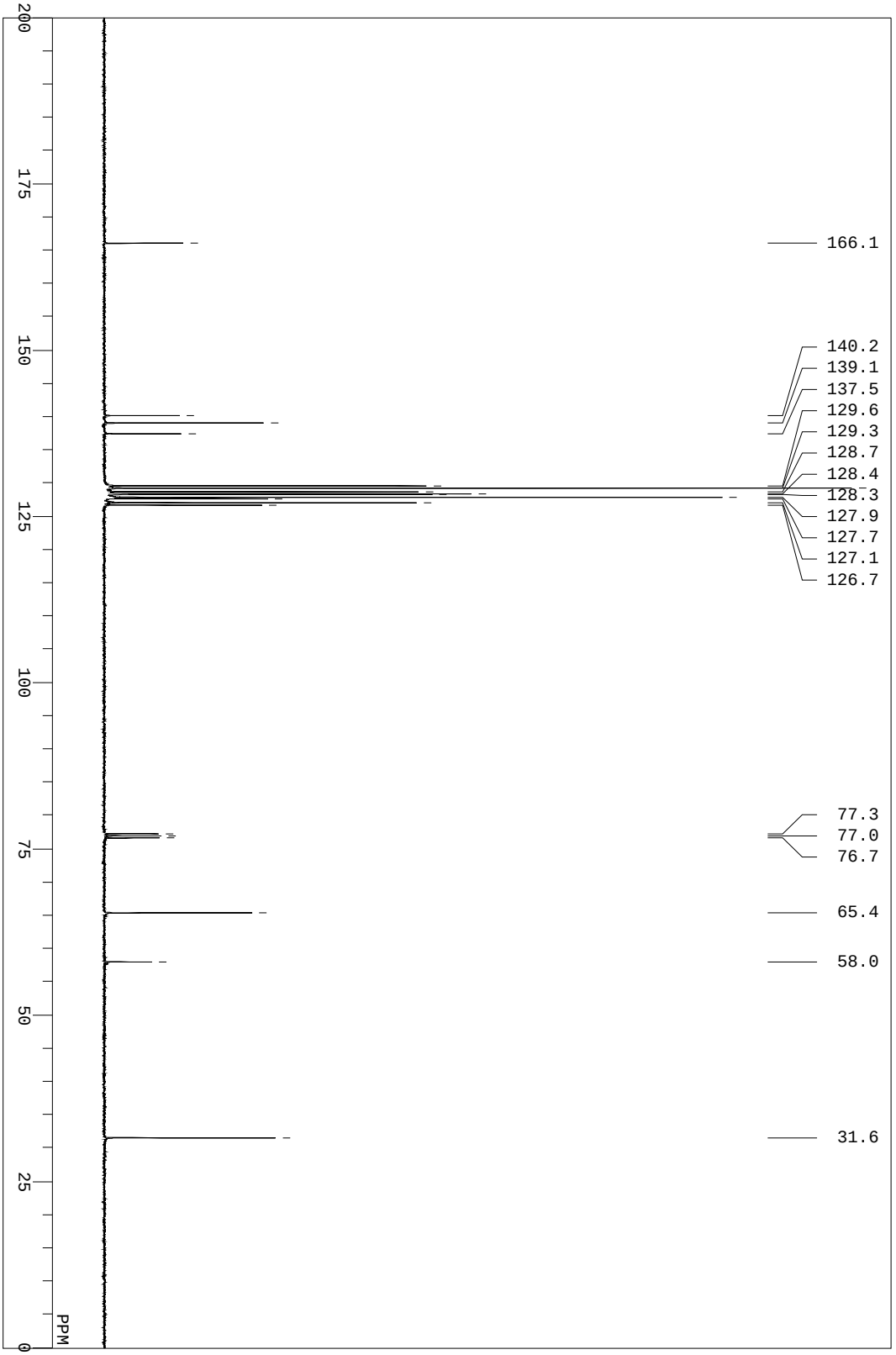

10
8
6
4
2
0
PPM
7.28
7.20
7.15
7.06
7.04
7.02
6.73
6.73
6.72
6.72
6.71
6.71
6.70
6.70
6.55
6.55
6.55
6.53
6.53
6.53
6.53
6.36
6.36
6.35
13.2
1.0
1.0
1.0
1.0
1.0
3.0
3.0
3.57
1.84
0.00
Me
O
N
CHPh2
N2
OMe
3g

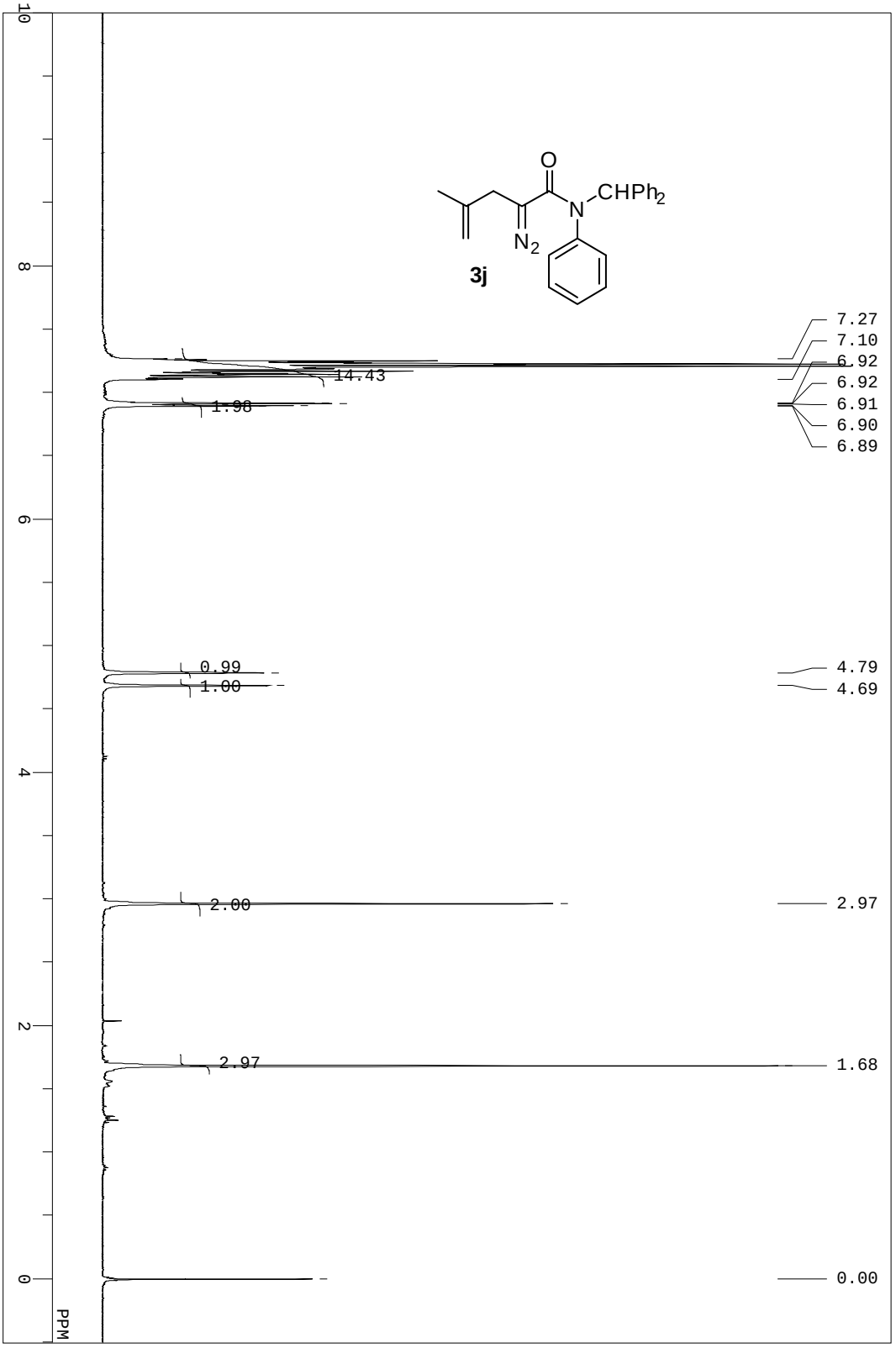

200
175
150
125
100
75
50
25
0
PPM
167.2
159.8
141.5
139.2
129.4
129.4
128.0
127.2
122.2
115.3
113.6
77.3
77.0
76.7
65.4
55.2
53.4
11.5

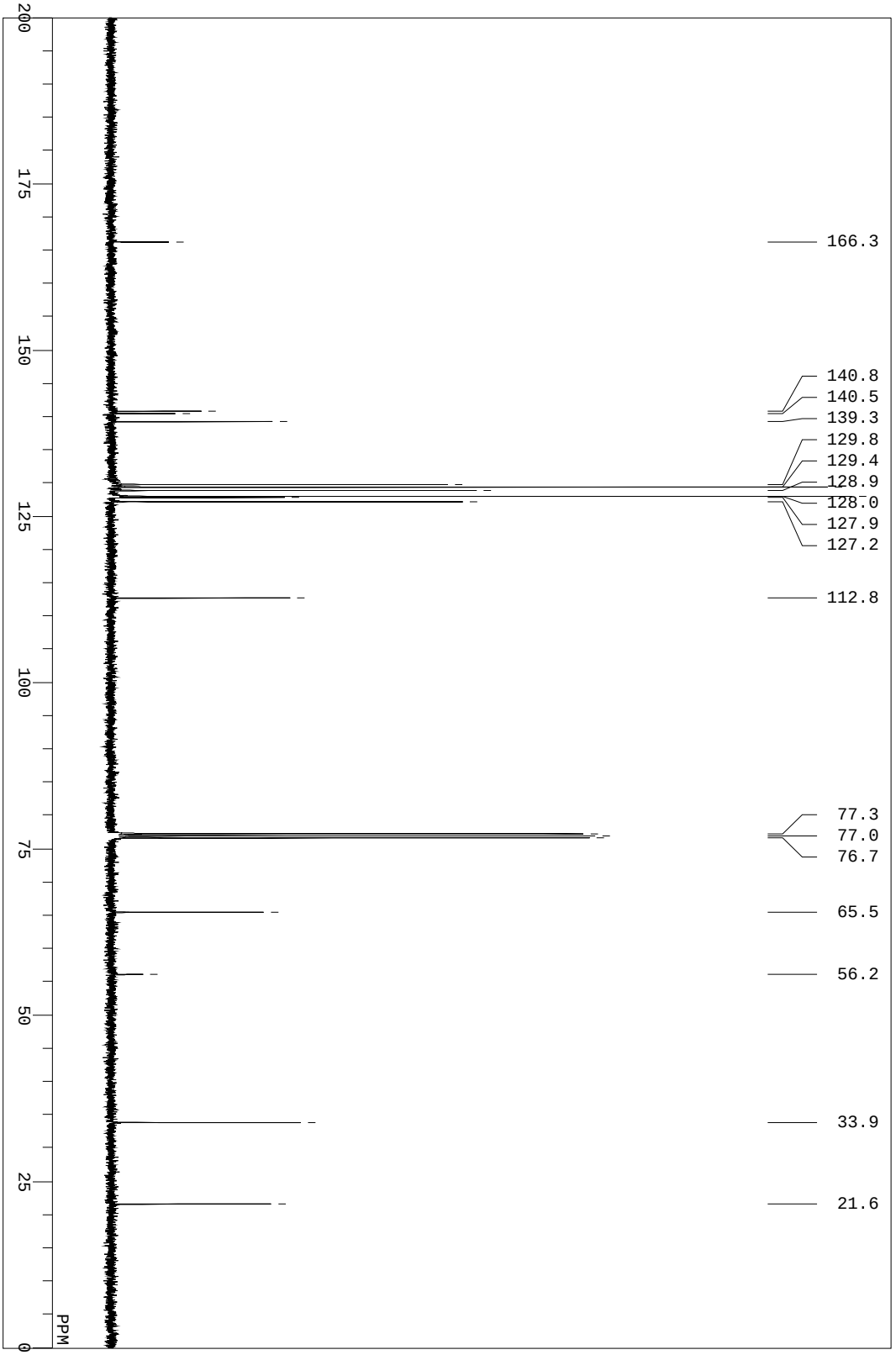

10
8
6
4
2
0
PPM
14.8
2.0
2.0
3.0
7.27
7.10
6.91
6.90
6.90
6.89
6.88
6.88
2.33
2.31
2.29
2.27
1.03
1.01
0.99
O
Et
N
CHPh2
N2
3h

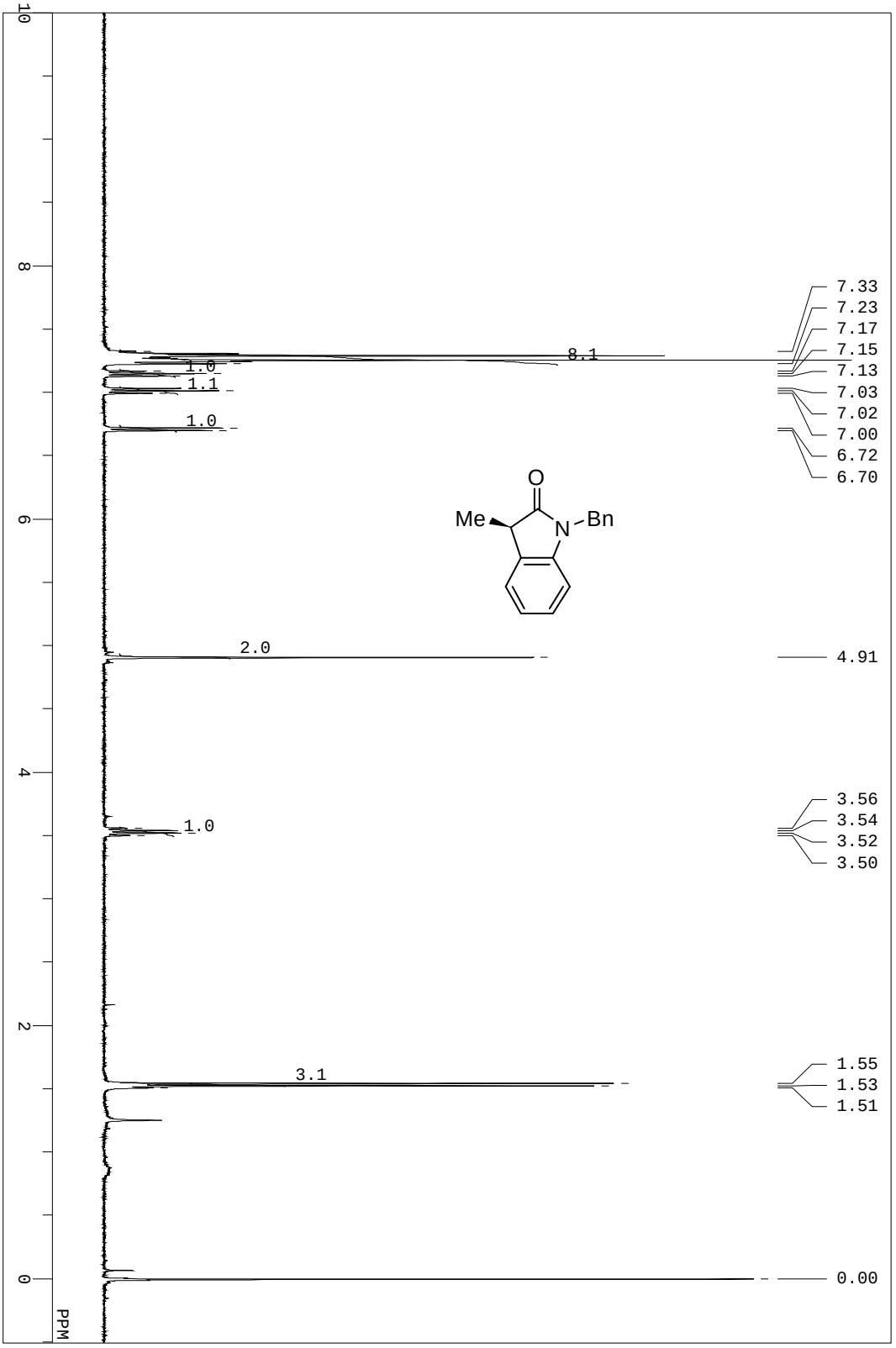

200
175
150
125
100
75
50
25
0
PPM
166.7
140.6
139.3
129.7
129.4
128.9
128.0
127.7
127.2
77.3
77.0
76.7
65.4
58.3
18.7
11.5

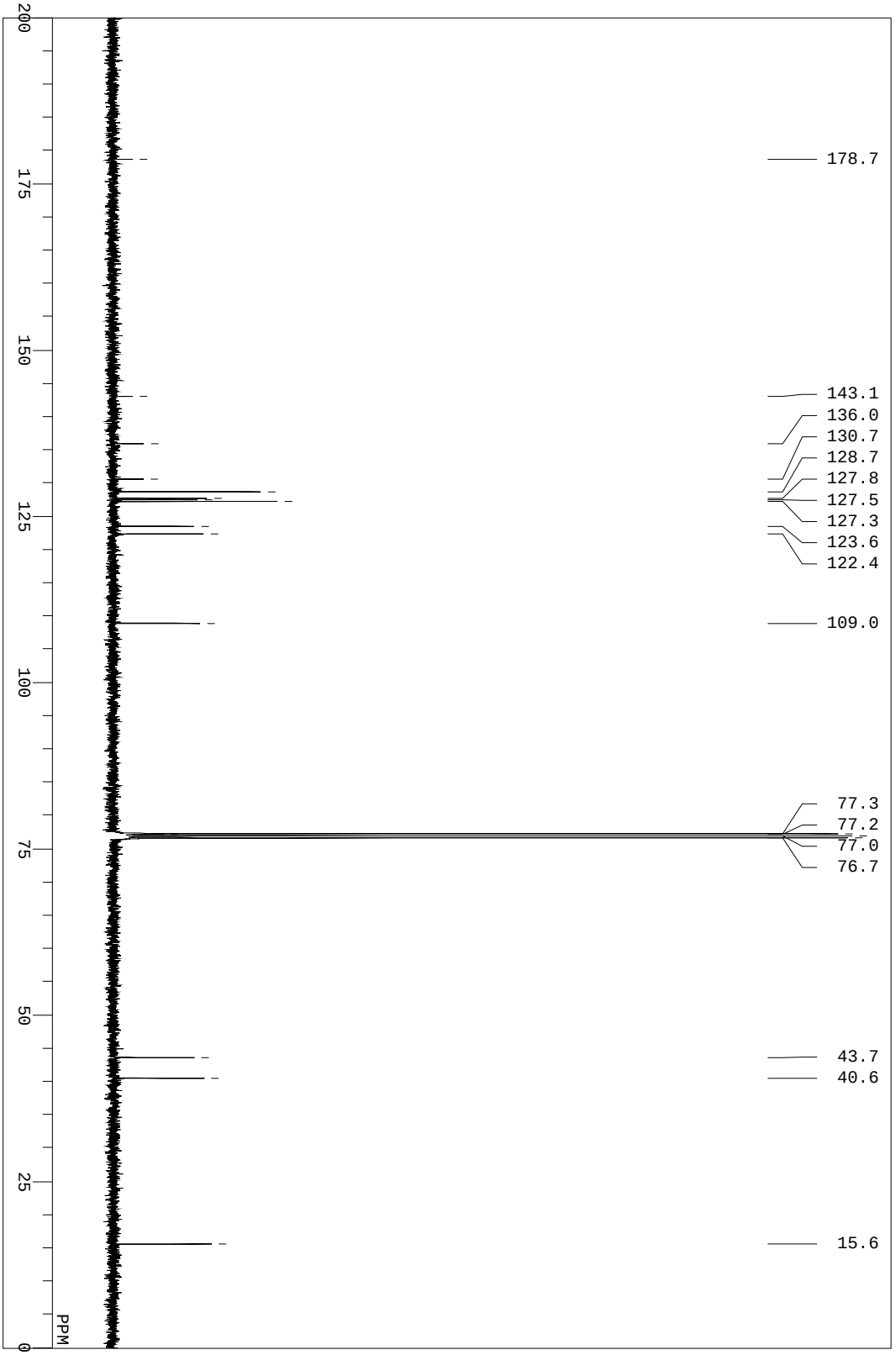

10
8
6
4
2
0
PPM
7.31
7.07
6.86
6.86
6.86
6.85
6.84
6.84
23.1
2.0
2.0
3.58
1.54
0.00
Bn
O
N
CHPh2
N2
3i

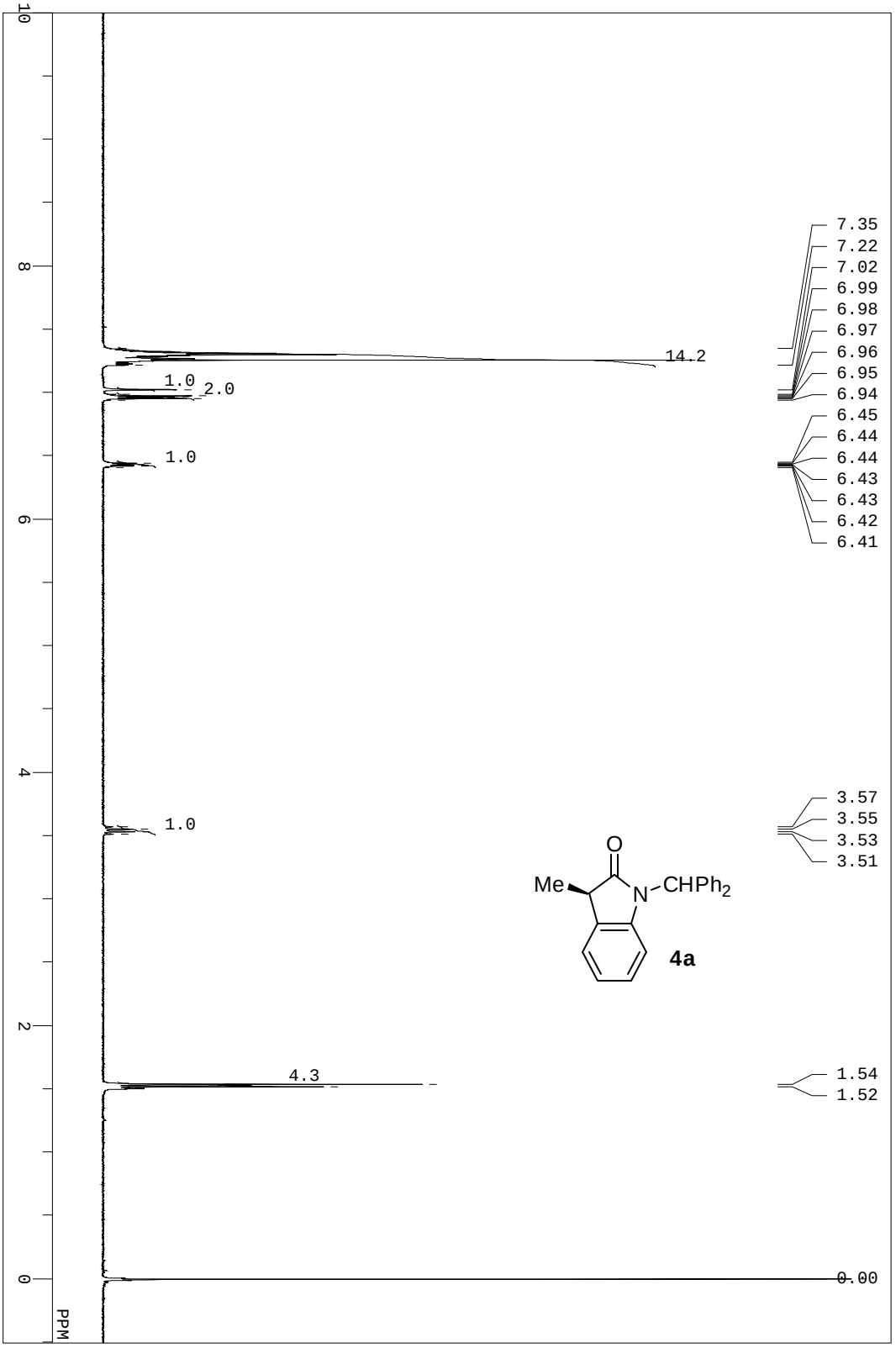

200
175
150
125
100
75
50
25
0
PPM
166.1
140.2
139.1
137.5
129.6
129.3
128.7
128.4
128.3
127.9
127.7
127.1
126.7
77.3
77.0
76.7
65.4
58.0
31.6

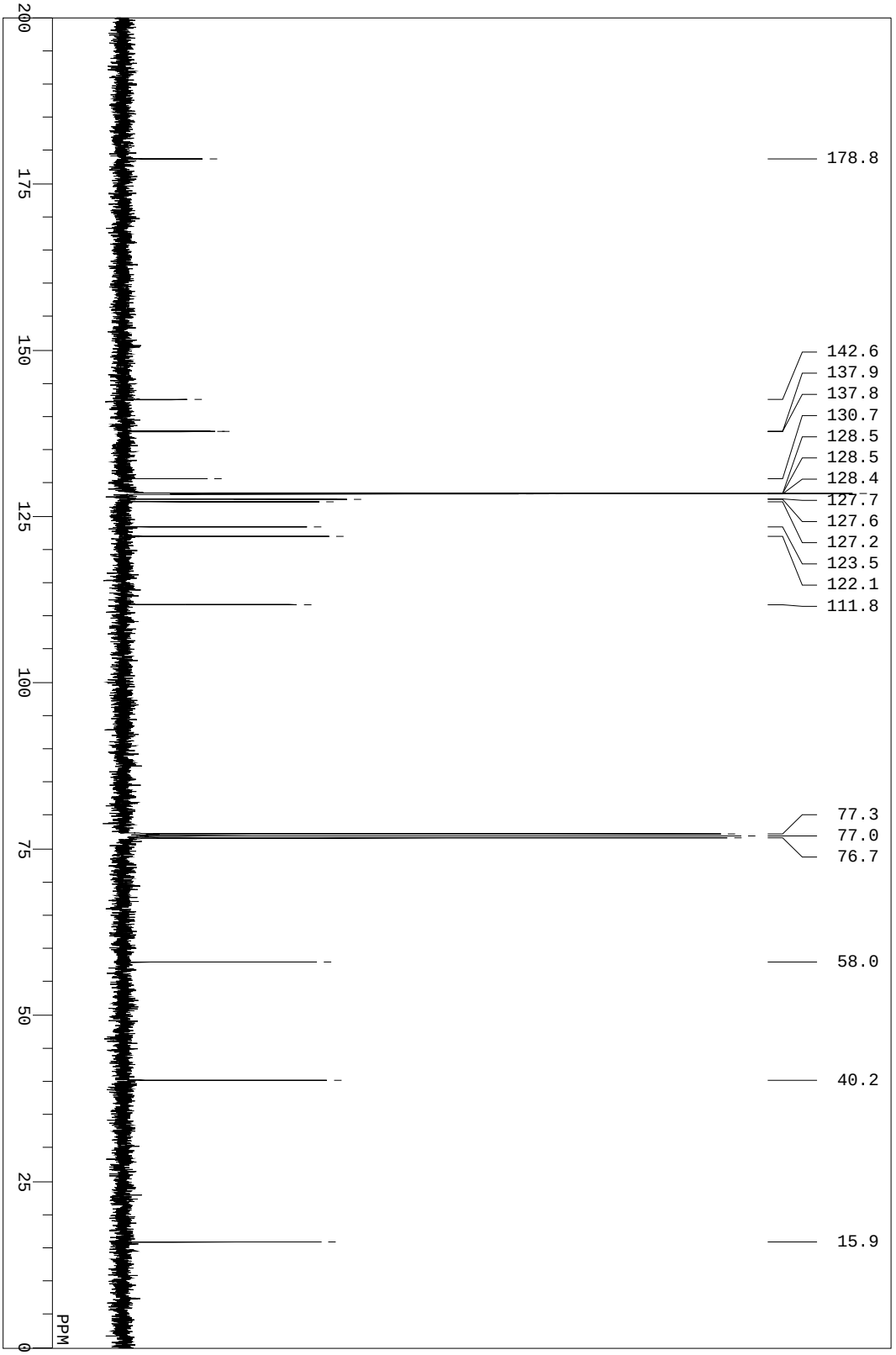

O
N
CHPh2
N2
3j
7.27
7.10
6.92
6.92
6.91
6.90
6.89
14.43
1.98
0.99
1.00
2.00
2.97
4.79
4.69
2.97
1.68
0.00
PPM

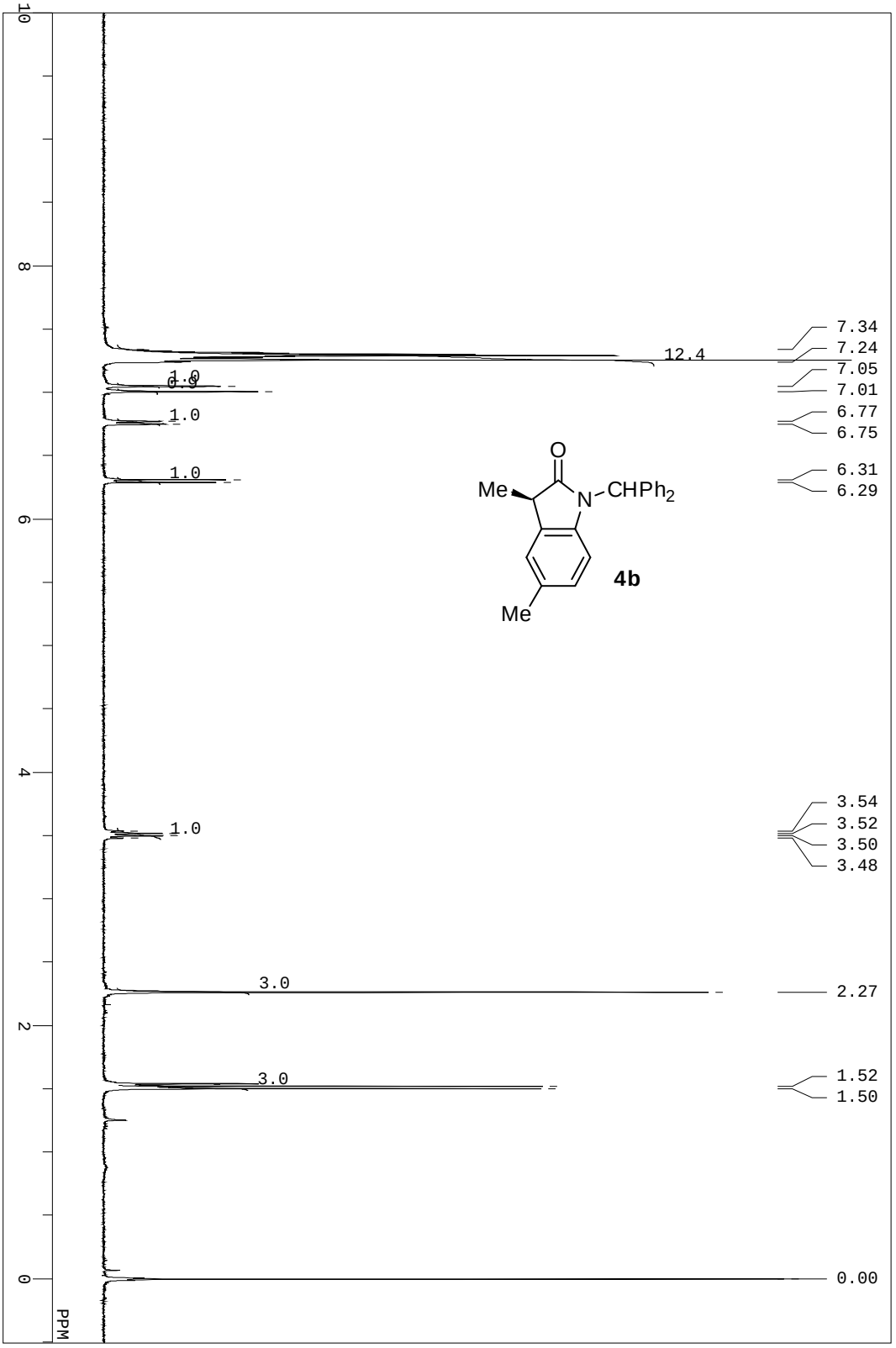

200
175
150
125
100
75
50
25
0
PPM
166.3
140.8
140.5
139.3
129.8
129.4
128.9
128.0
127.9
127.2
112.8
77.3
77.0
76.7
65.5
56.2
33.9
21.6

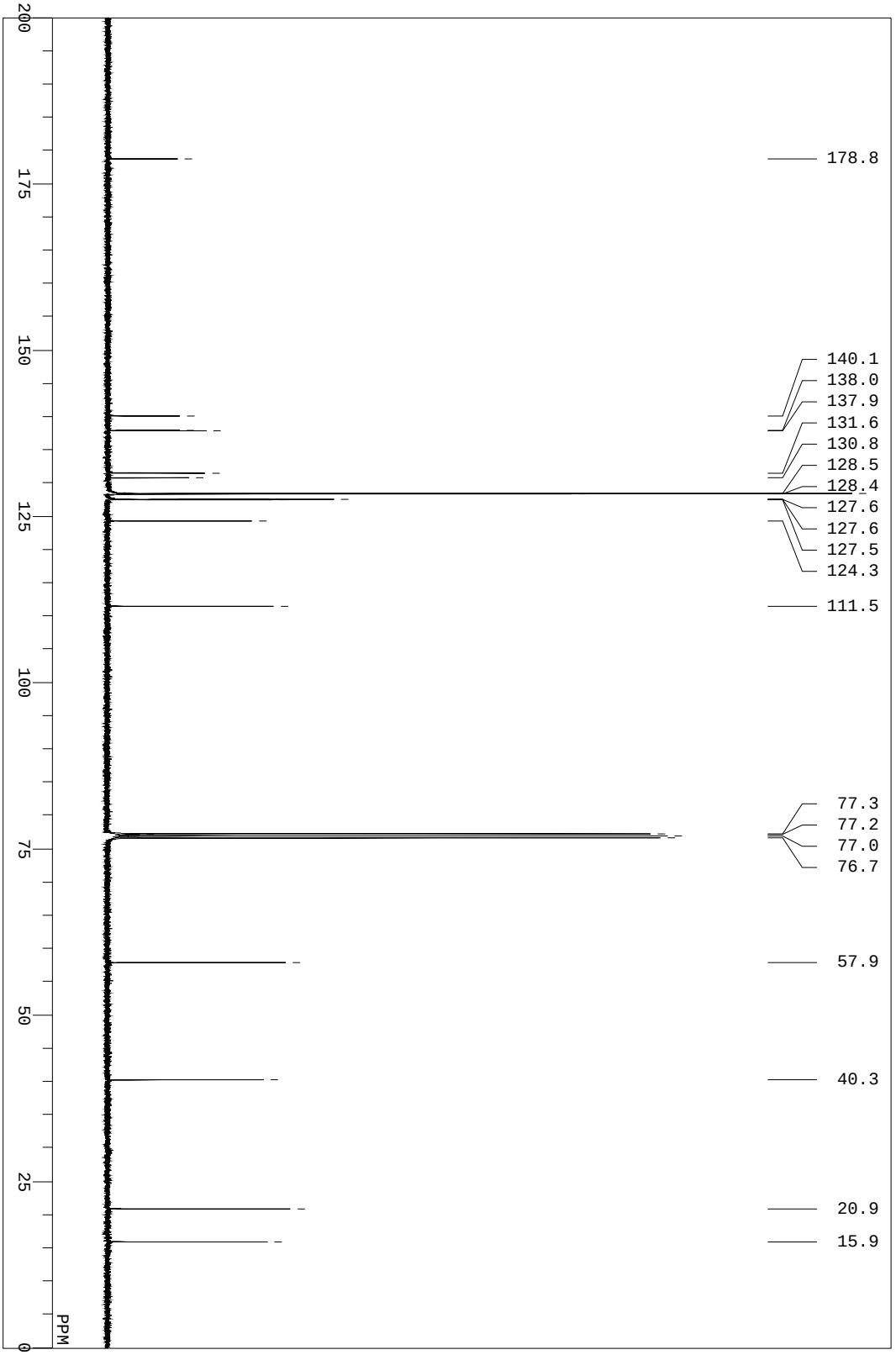

10
8
6
4
2
0
PPM
7.33
7.23
7.17
7.15
7.13
7.03
7.02
7.00
6.72
6.70
8.1
1.0
1.1
1.0
2.0
4.91
1.0
3.56
3.54
3.52
3.50
3.1
1.55
1.53
1.51
0.00
O
Me
N
Bn

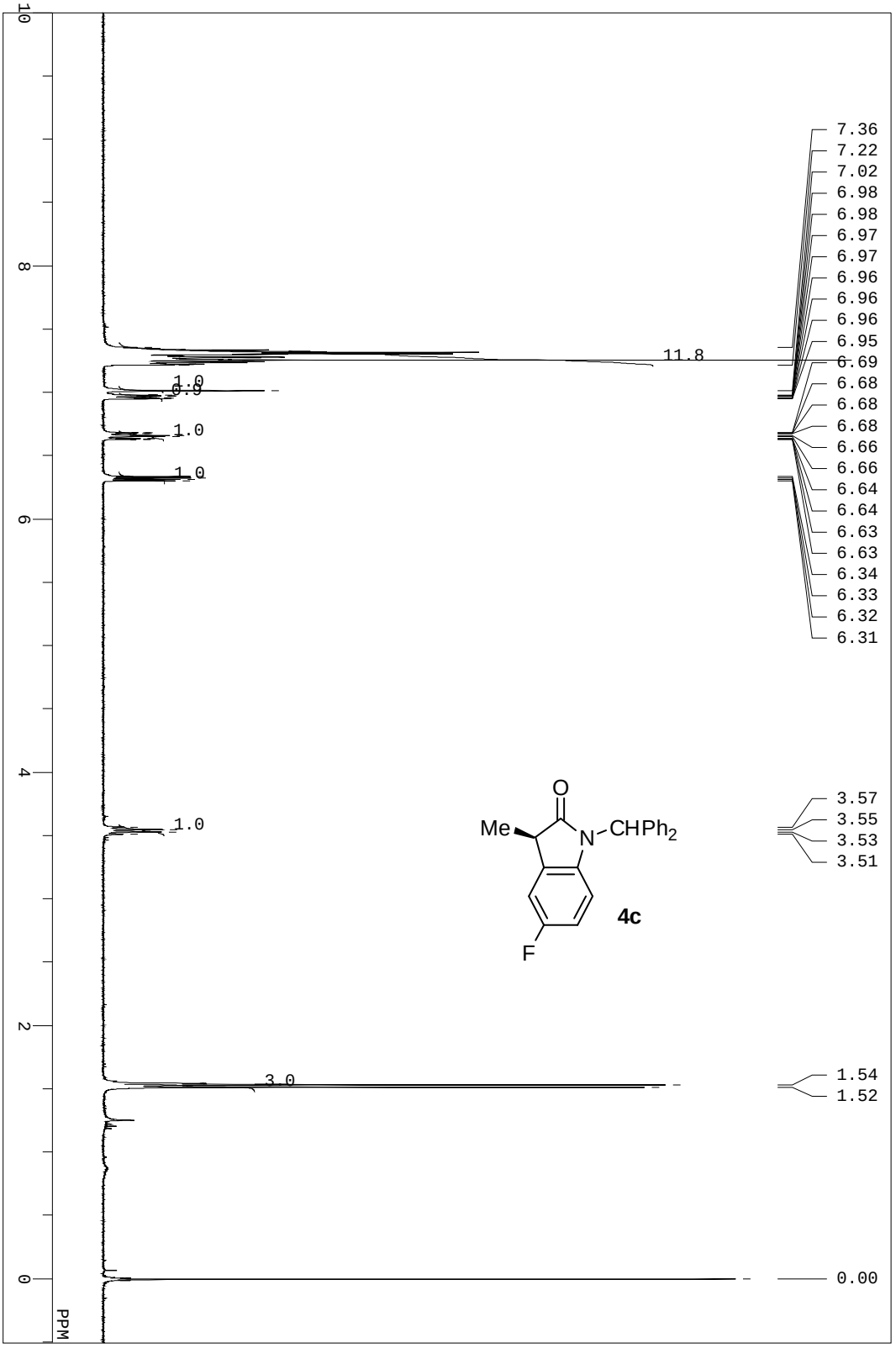

200
175
150
125
100
75
50
25
0
PPM
178.7
143.1
136.0
130.7
128.7
127.8
127.5
127.3
123.6
122.4
109.0
77.3
77.2
77.0
76.7
43.7
40.6
15.6

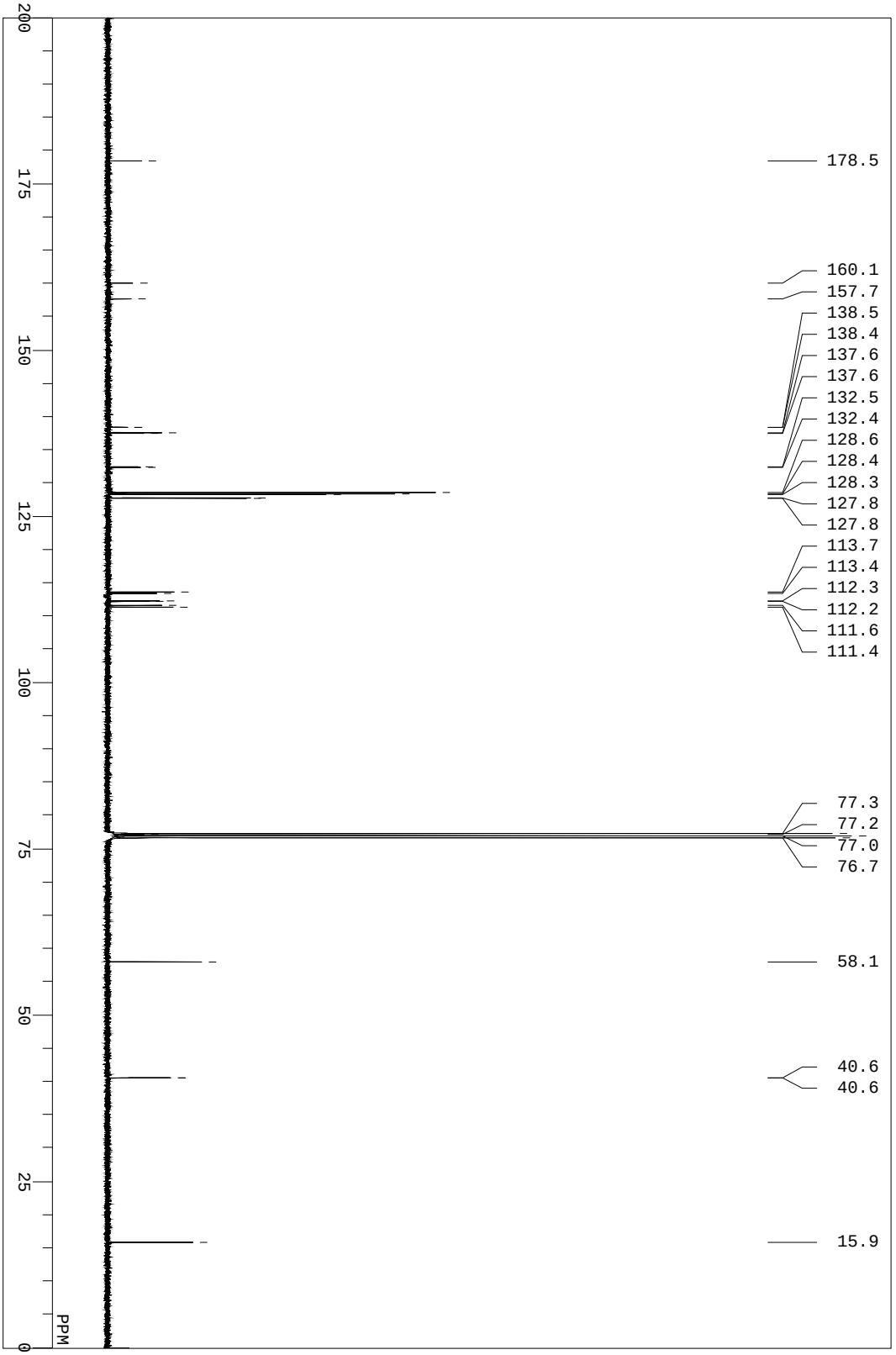

10
8
6
4
2
0
PPM
7.35
7.22
7.02
6.99
6.98
6.97
6.96
6.95
6.94
6.45
6.44
6.44
6.43
6.43
6.42
6.41
3.57
3.55
3.53
3.51
1.54
1.52
0.00
14.2
1.0
2.0
1.0
1.0
4.3
O
Me
N
CHPh2
4a

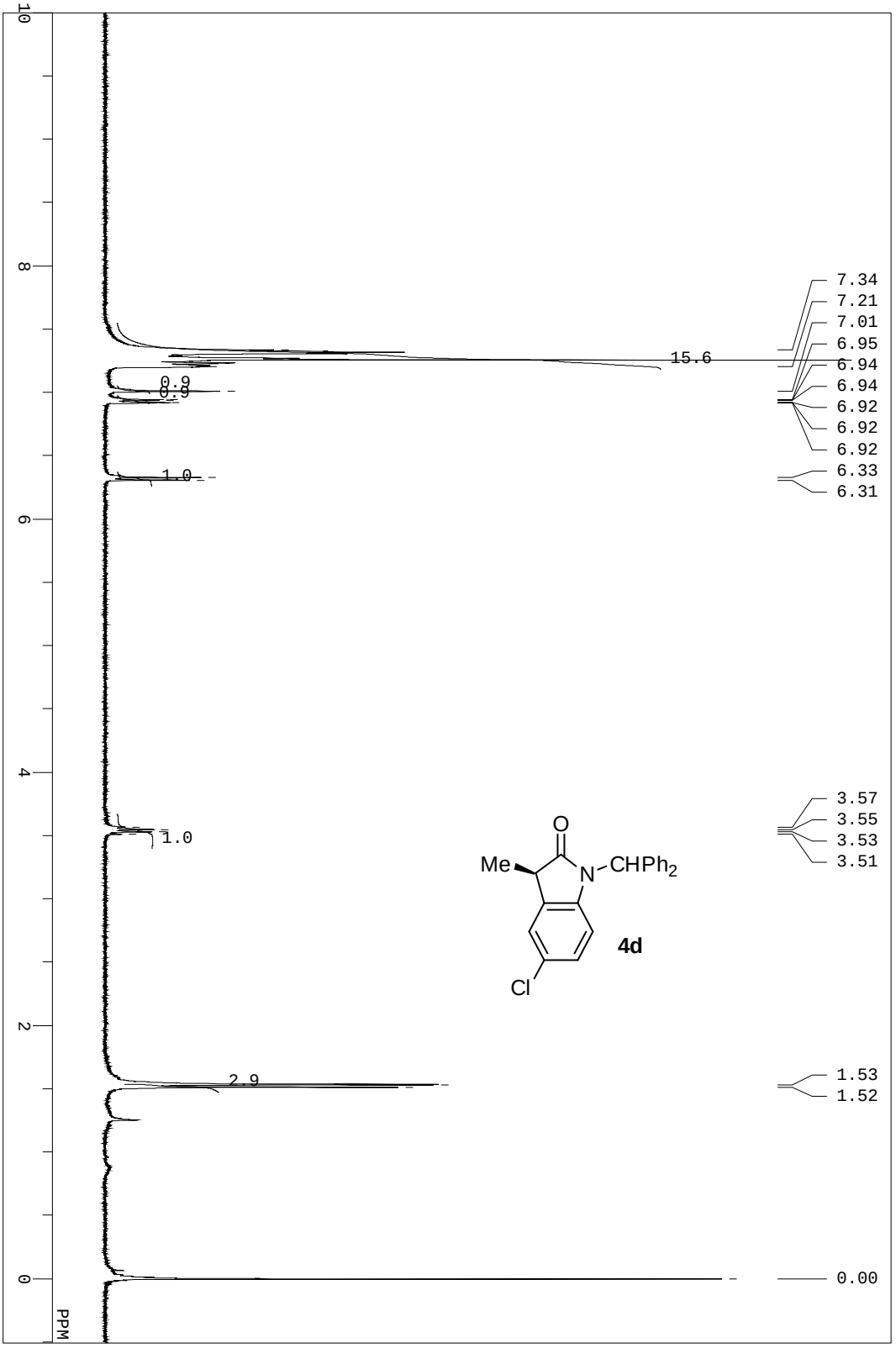

200
175
150
125
100
75
50
25
0
PPM
178.8
142.6
137.9
137.8
130.7
128.5
128.5
128.4
127.7
127.6
127.2
123.5
122.1
111.8
77.3
77.0
76.7
58.0
40.2
15.9

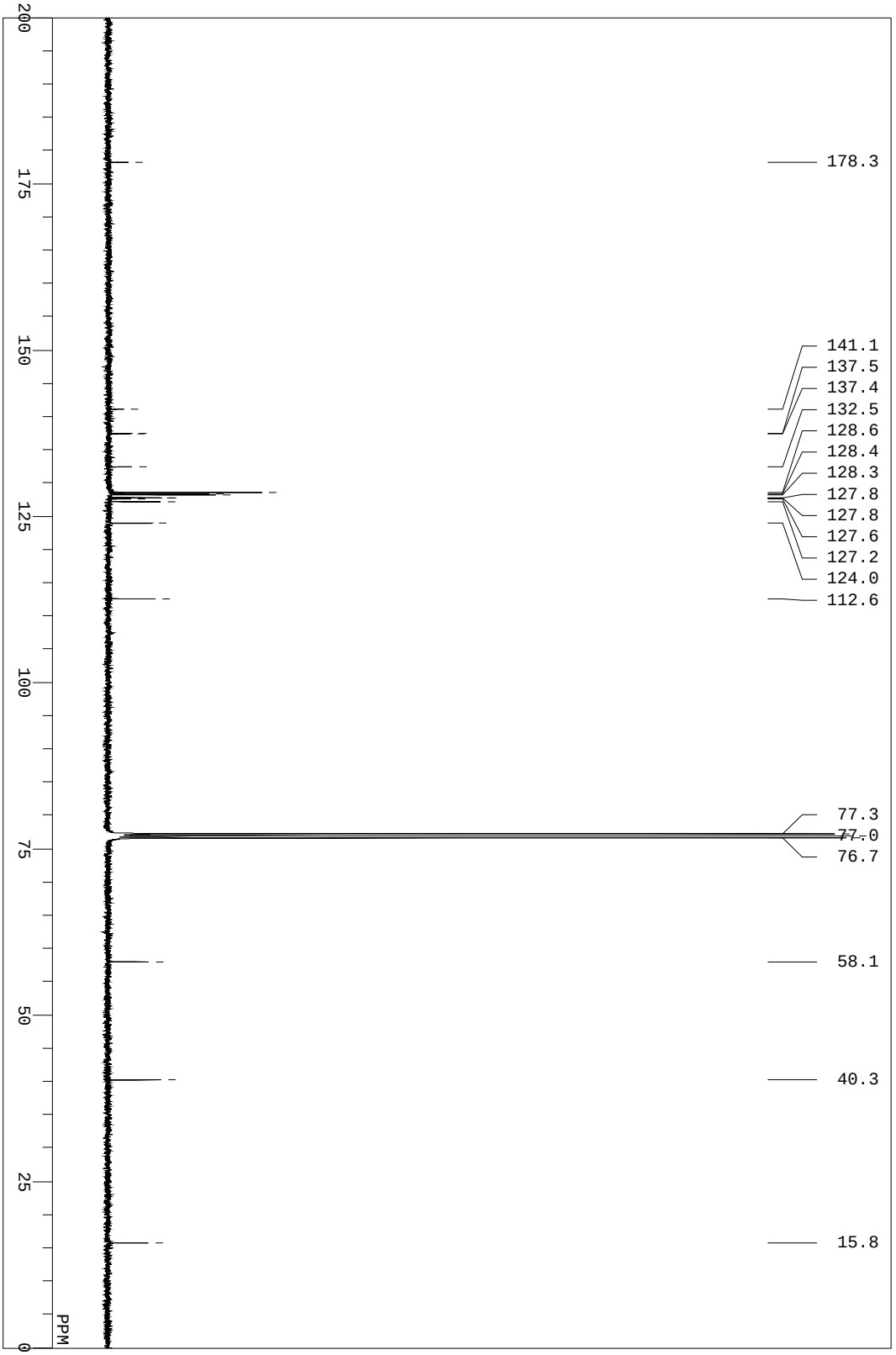

10
8
6
4
2
0
PPM
7.34
7.24
7.05
7.01
6.77
6.75
6.31
6.29
3.54
3.52
3.50
3.48
2.27
1.52
1.50
0.00
12.4
1.0
1.0
1.0
1.0
3.0
3.0
O
Me
N
CHPh2
Me
4b

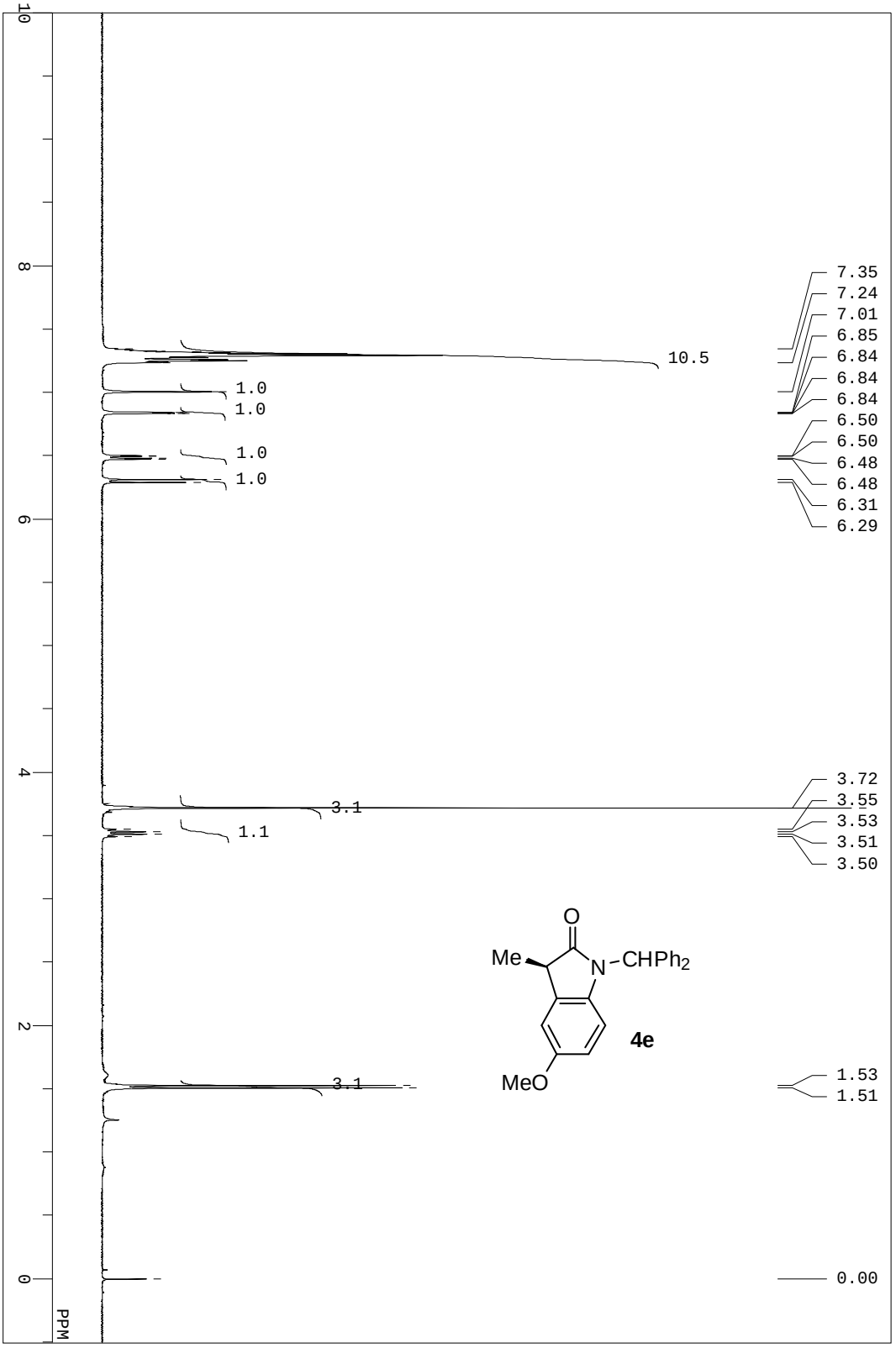

200
175
150
125
100
75
50
25
0
PPM
178.8
140.1
138.0
137.9
131.6
130.8
128.5
128.4
127.6
127.6
127.5
124.3
111.5
77.3
77.2
77.0
76.7
57.9
40.3
20.9
15.9

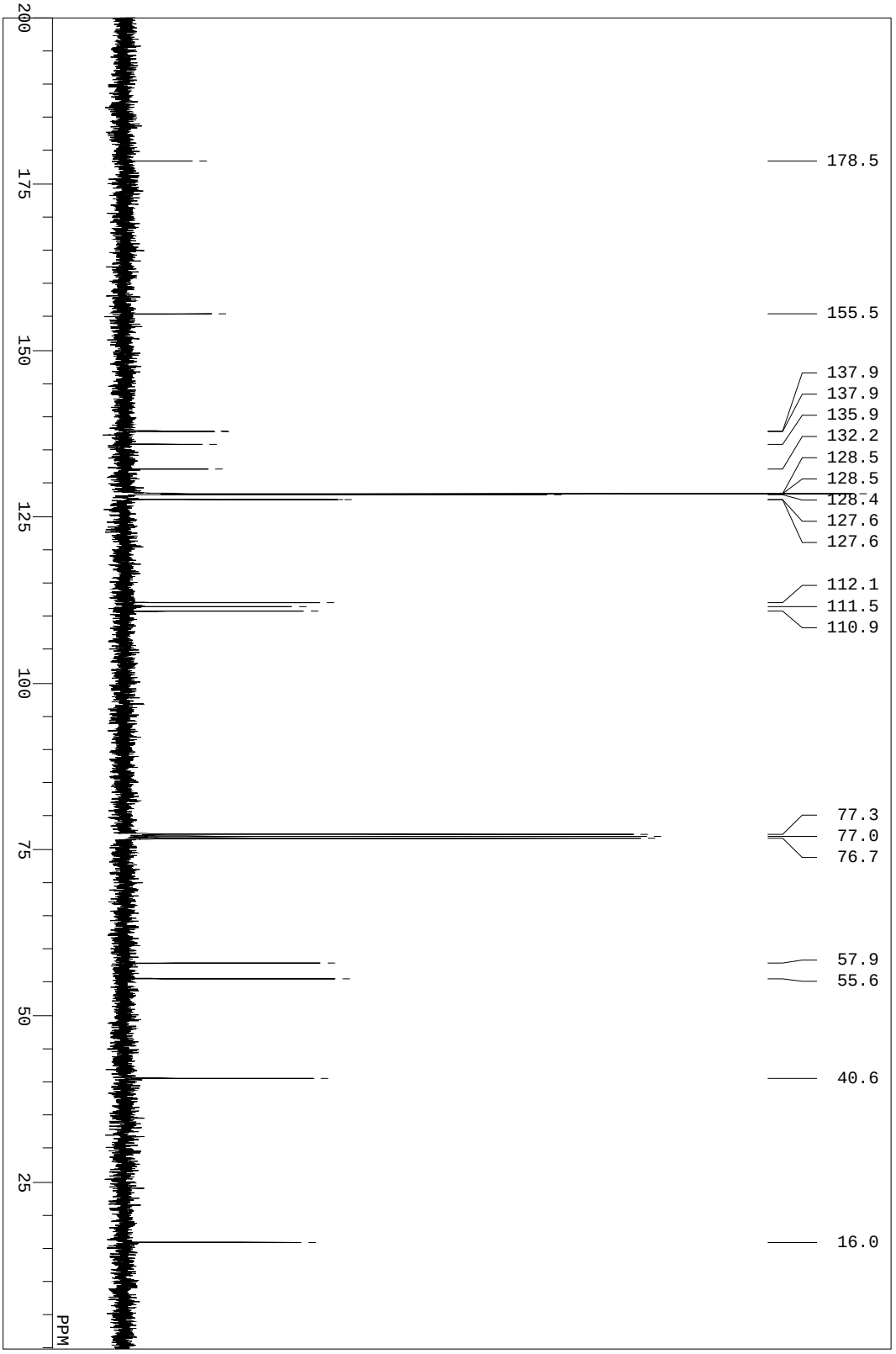

10
8
6
4
2
0
PPM
7.36
7.22
7.02
6.98
6.98
6.97
6.97
6.96
6.96
6.96
6.95
6.69
6.68
6.68
6.68
6.66
6.66
6.64
6.64
6.63
6.63
6.34
6.33
6.32
6.31
11.8
1.0
0.9
1.0
1.0
1.0
3.0
3.57
3.55
3.53
3.51
1.54
1.52
0.00
O
Me
N
CHPh2
F
4c

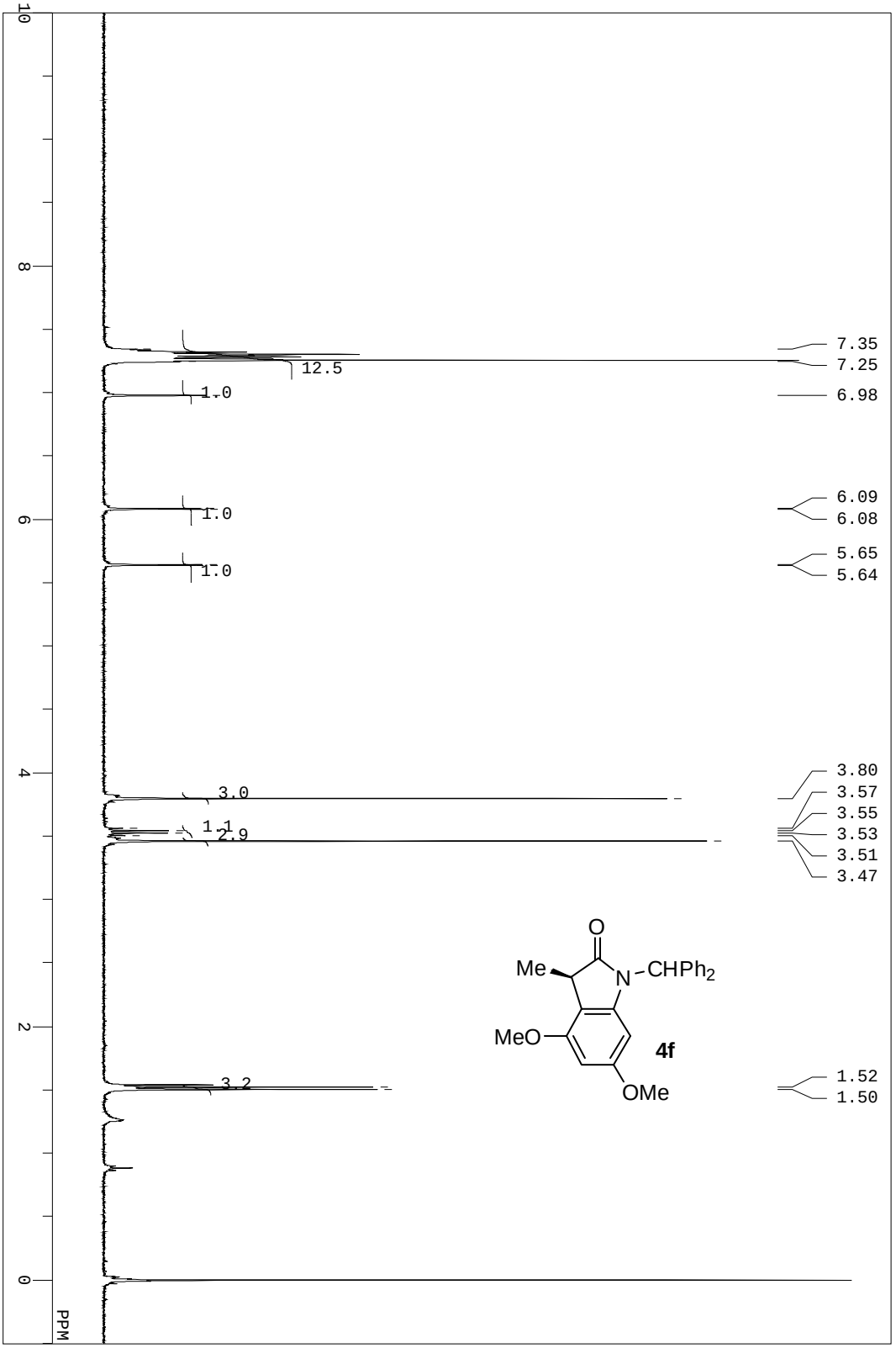

200
175
150
125
100
75
50
25
0
PPM
178.5
160.1
157.7
138.5
138.4
137.6
137.6
132.5
132.4
128.6
128.4
128.3
127.8
127.8
113.7
113.4
112.3
112.2
111.6
111.4
77.3
77.2
77.0
76.7
58.1
40.6
40.6
15.9

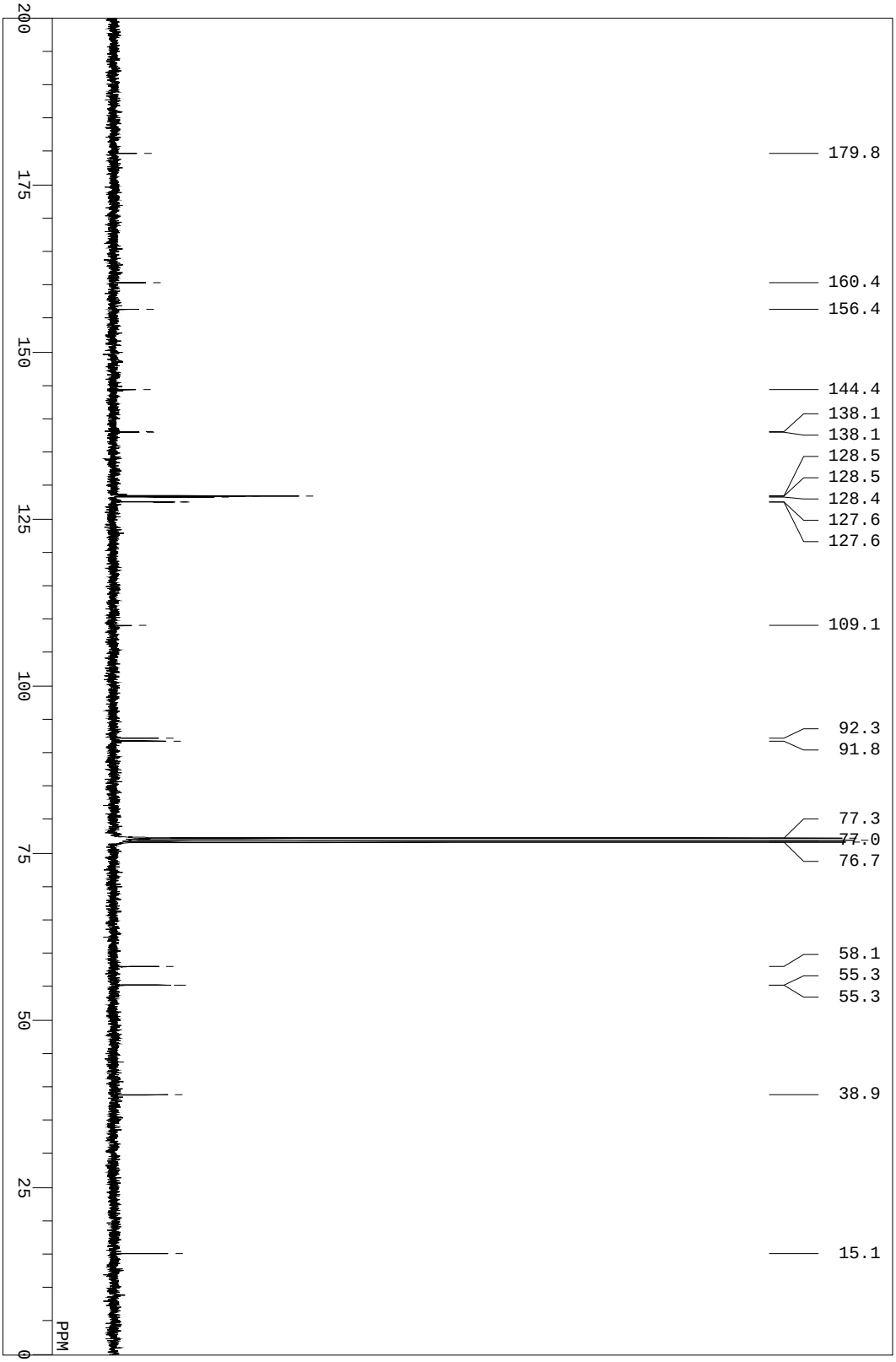

10
8
6
4
2
0
PPM
7.34
7.21
7.01
6.95
6.94
6.94
6.92
6.92
6.92
6.33
6.31
15.6
0.9
0.9
1.0
1.0
2.9
3.57
3.55
3.53
3.51
1.53
1.52
0.00
O
Me
N
CHPh2
Cl
4d

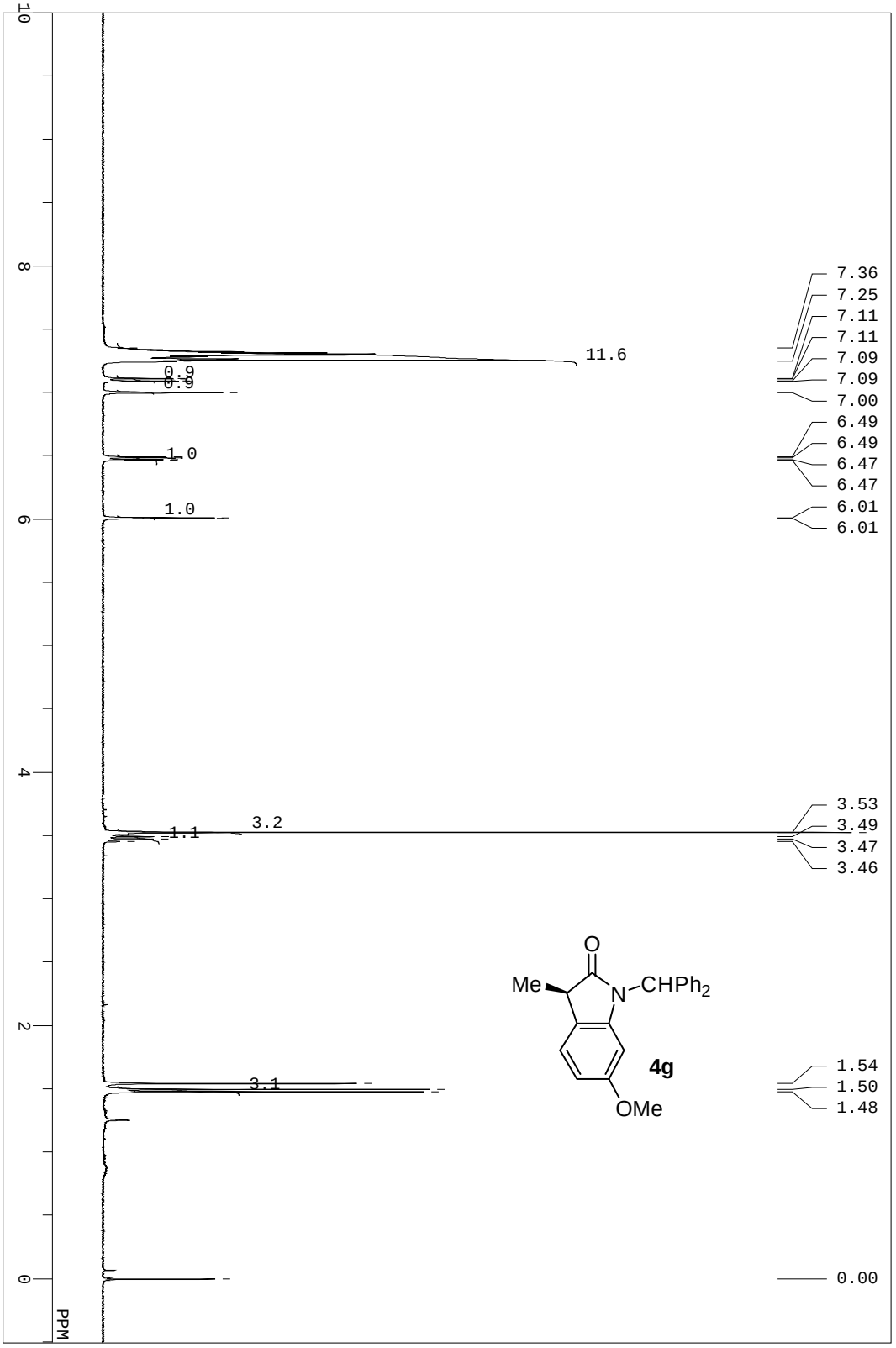

178.3
141.1
137.5
137.4
132.5
128.6
128.4
128.3
127.8
127.8
127.6
127.2
124.0
112.6
77.3
77.0
76.7
58.1
40.3
15.8
PPM
200
175
150
125
100
75
50
25
0

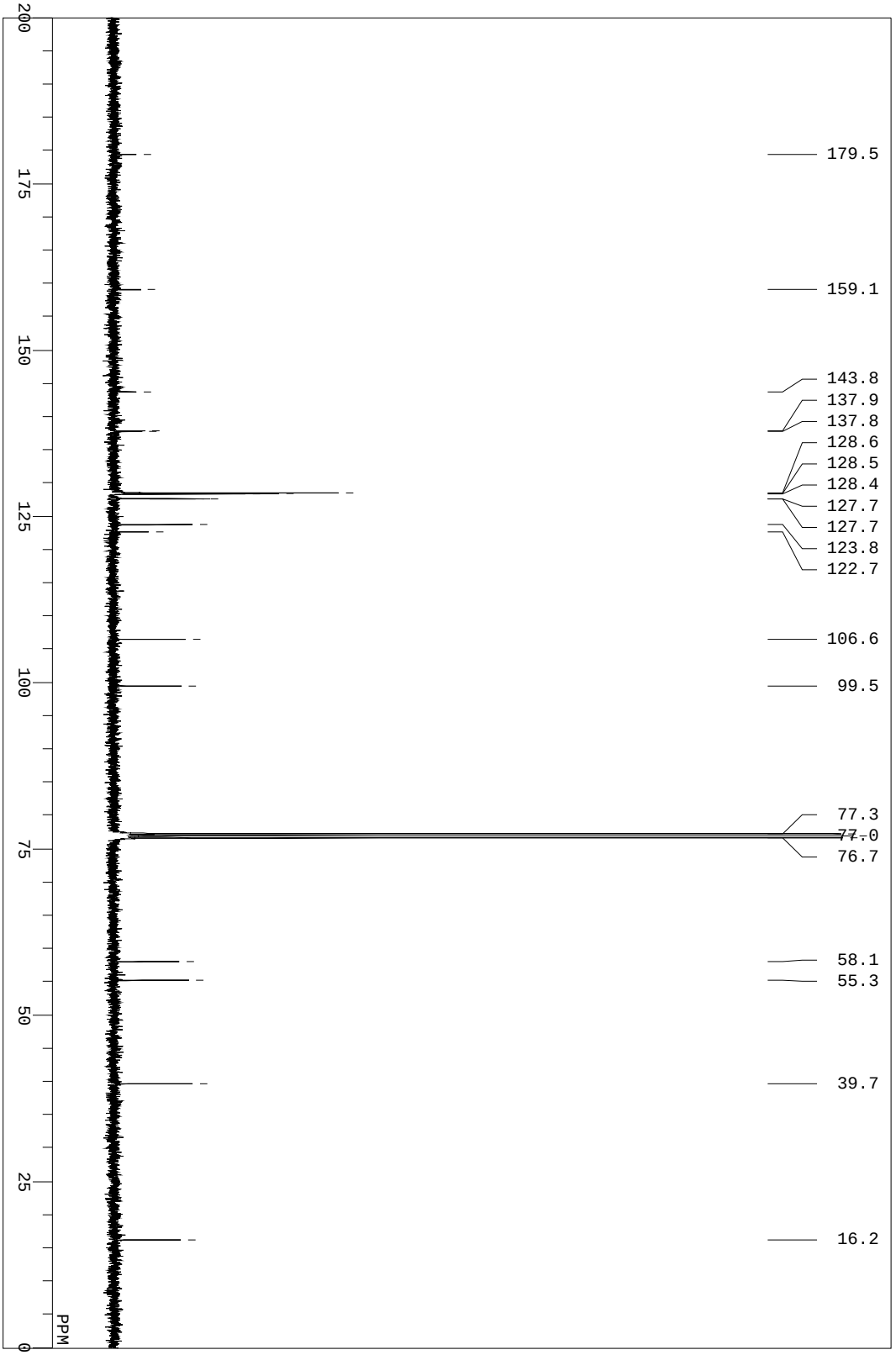

10
8
6
4
2
0
PPM
7.35
7.24
7.01
6.85
6.84
6.84
6.84
6.50
6.50
6.48
6.48
6.31
6.29
10.5
1.0
1.0
1.0
1.0
3.72
3.55
3.53
3.51
3.50
3.1
1.1
3.1
1.53
1.51
0.00
O
Me
N
CHPh2
MeO
4e

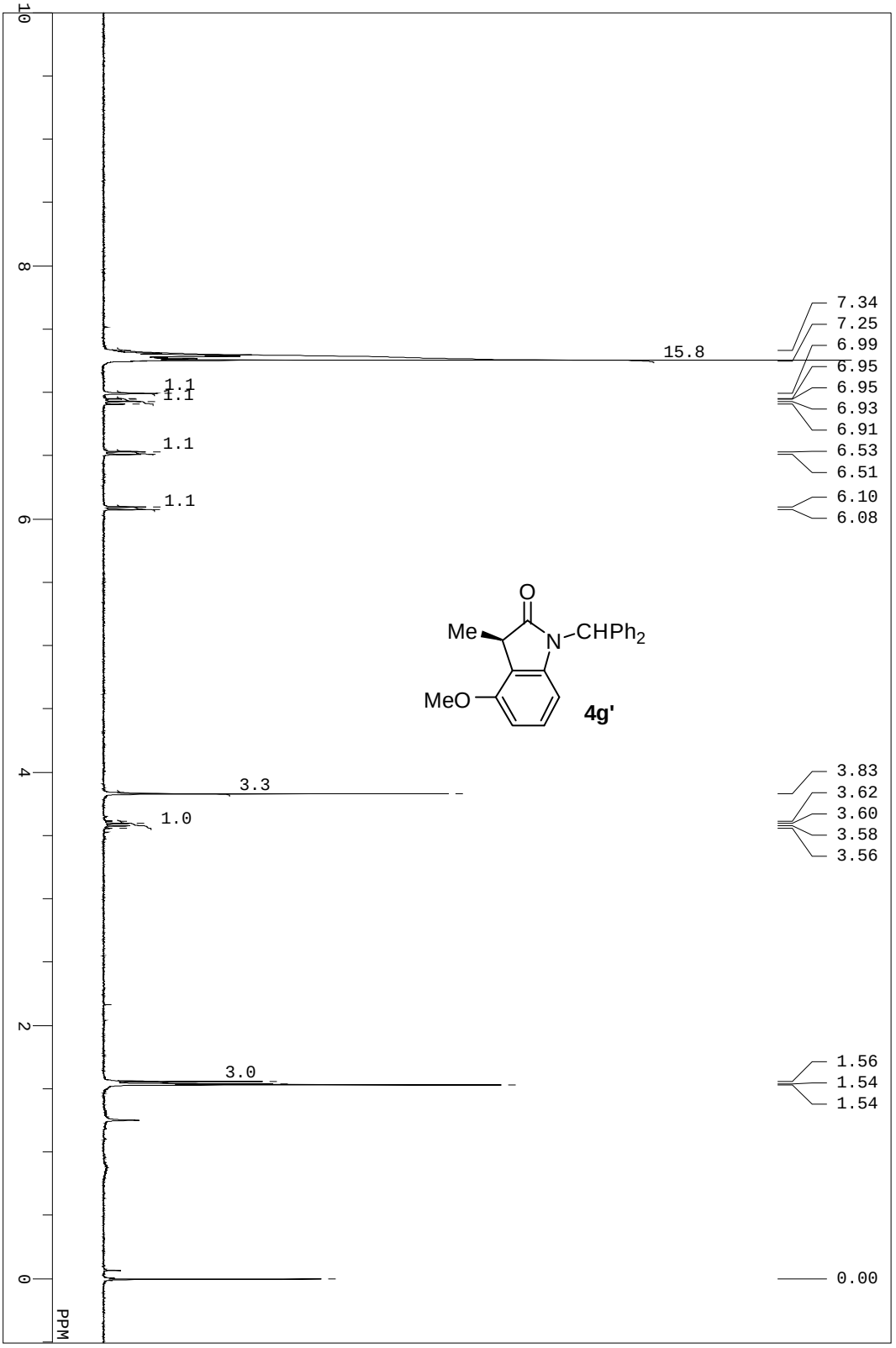

200
175
150
125
100
75
50
25
PPM
178.5
155.5
137.9
137.9
135.9
132.2
128.5
128.5
128.4
127.6
127.6
112.1
111.5
110.9
77.3
77.0
76.7
57.9
55.6
40.6
16.0

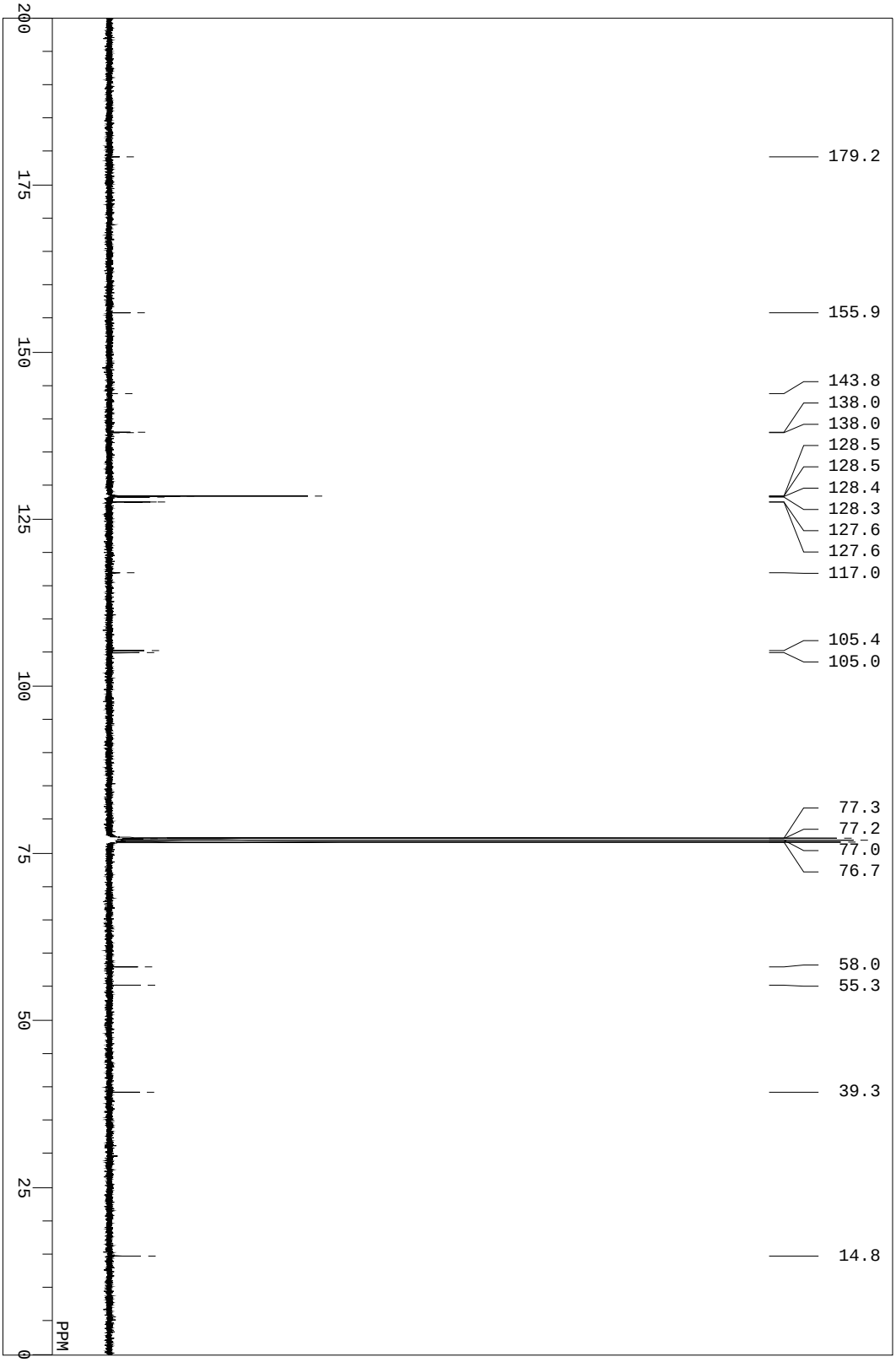

10
8
6
4
2
0
PPM
12.5
1.0
1.0
1.0
3.0
1.1
2.9
3.2
7.35
7.25
6.98
6.09
6.08
5.65
5.64
3.80
3.57
3.55
3.53
3.51
3.47
1.52
1.50
O
Me
N
CHPh2
MeO
OMe
4f

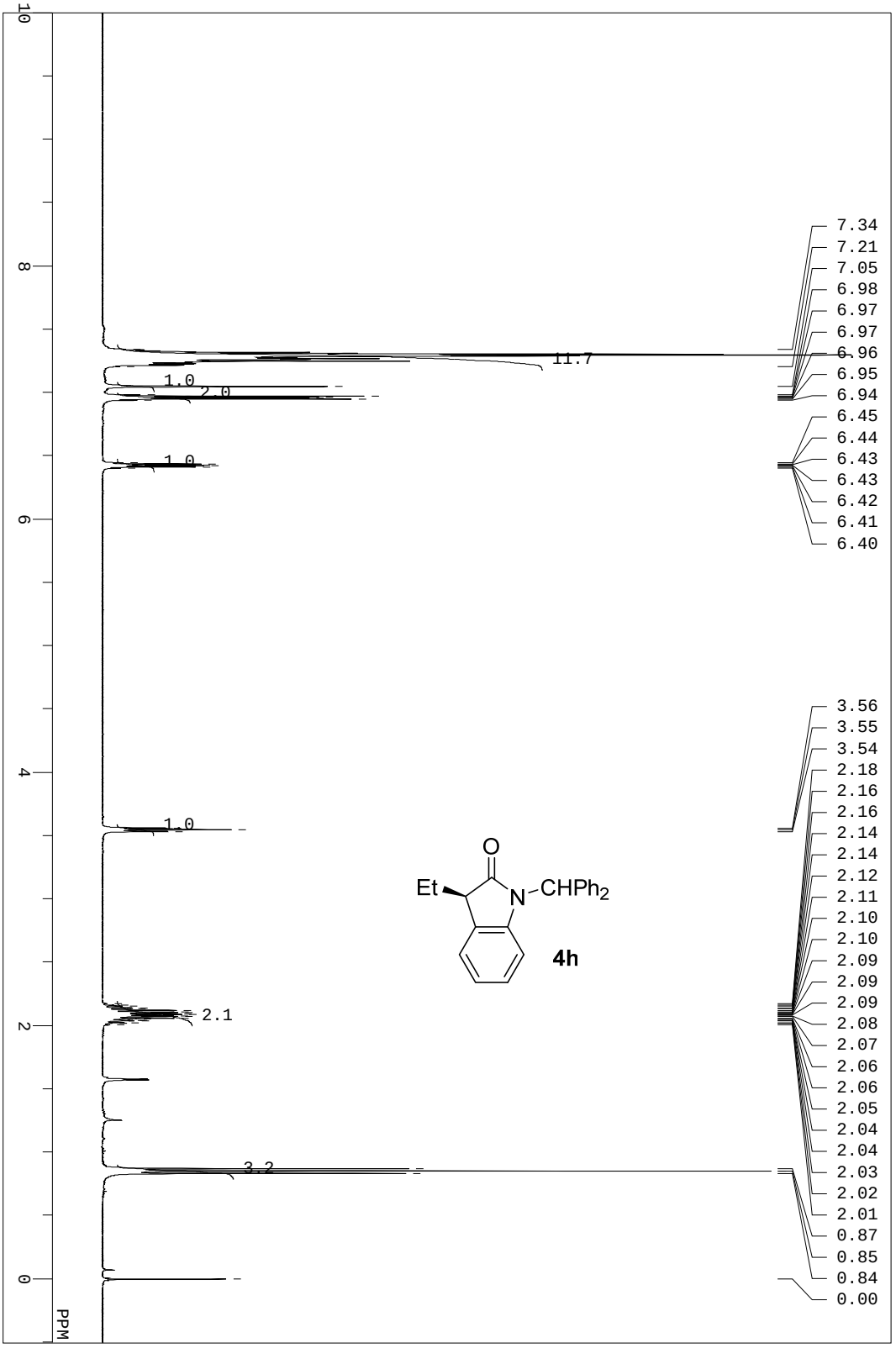

200
175
150
125
100
75
50
25
0
PPM
179.8
160.4
156.4
144.4
138.1
138.1
128.5
128.5
128.4
127.6
127.6
109.1
92.3
91.8
77.3
77.0
76.7
58.1
55.3
55.3
38.9
15.1

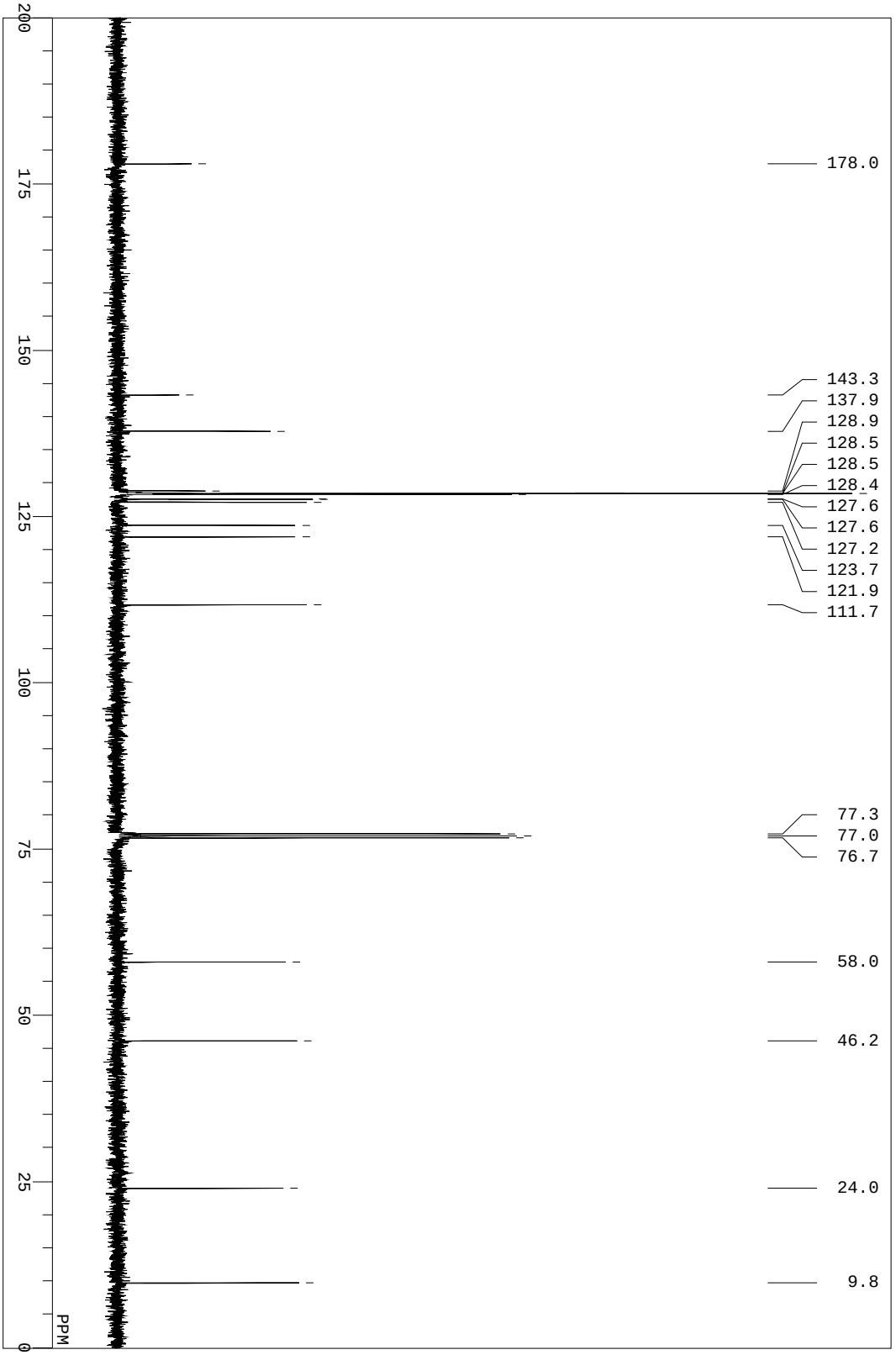

10
8
6
4
2
0
PPM
11.6
0.9
0.9
1.0
1.0
3.2
1.1
3.1
0.00
7.36
7.25
7.11
7.11
7.09
7.09
7.00
6.49
6.49
6.47
6.47
6.01
6.01
3.53
3.49
3.47
3.46
1.54
1.50
1.48
O
Me
N
CHPh2
OMe
4g

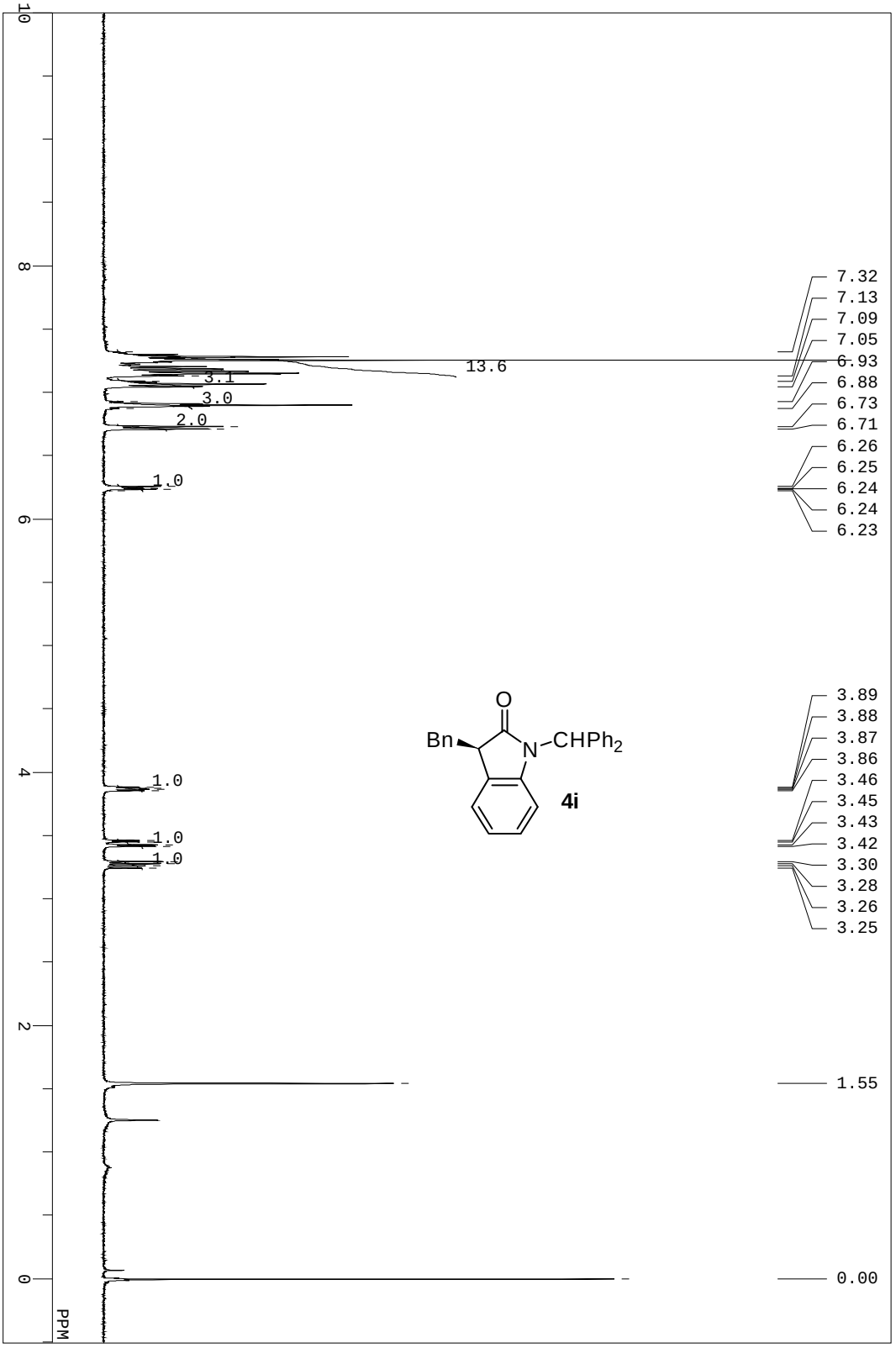

200
175
150
125
100
75
50
25
0
PPM
179.5
159.1
143.8
137.9
137.8
128.6
128.5
128.4
127.7
127.7
123.8
122.7
106.6
99.5
77.3
77.0
76.7
58.1
55.3
39.7
16.2

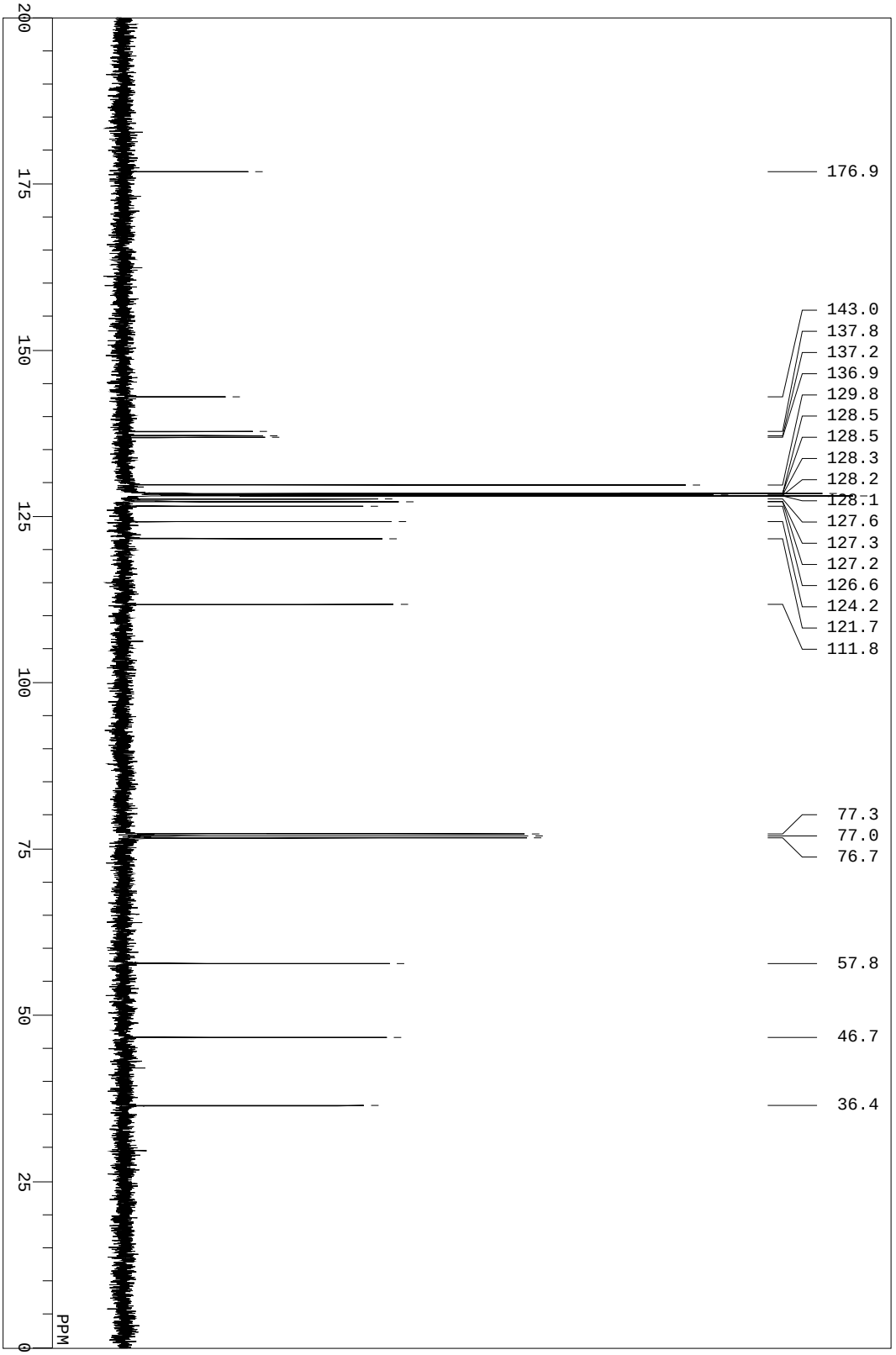

10
8
6
4
2
0
PPM
7.34
7.25
6.99
6.95
6.95
6.93
6.91
6.53
6.51
6.10
6.08
3.83
3.62
3.60
3.58
3.56
1.56
1.54
1.54
0.00
15.8
1.1
1.1
1.1
1.1
3.3
1.0
3.0
O
Me
N
CHPh2
MeO
4g'

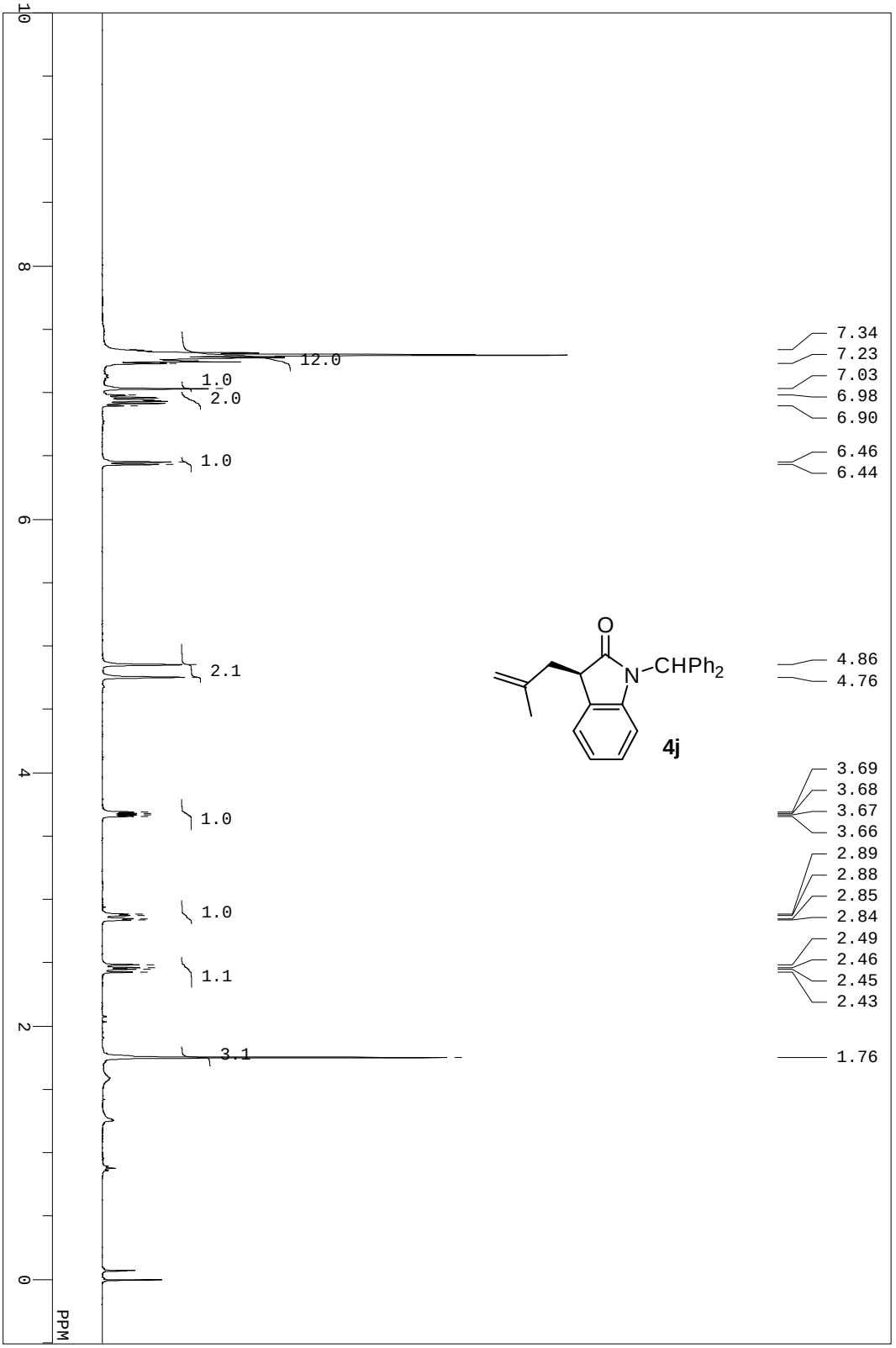

179.2
155.9
143.8
138.0
138.0
128.5
128.5
128.4
128.3
127.6
127.6
117.0
105.4
105.0
77.3
77.2
77.0
76.7
58.0
55.3
39.3
14.8
200
175
150
125
100
75
50
25
0
PPM

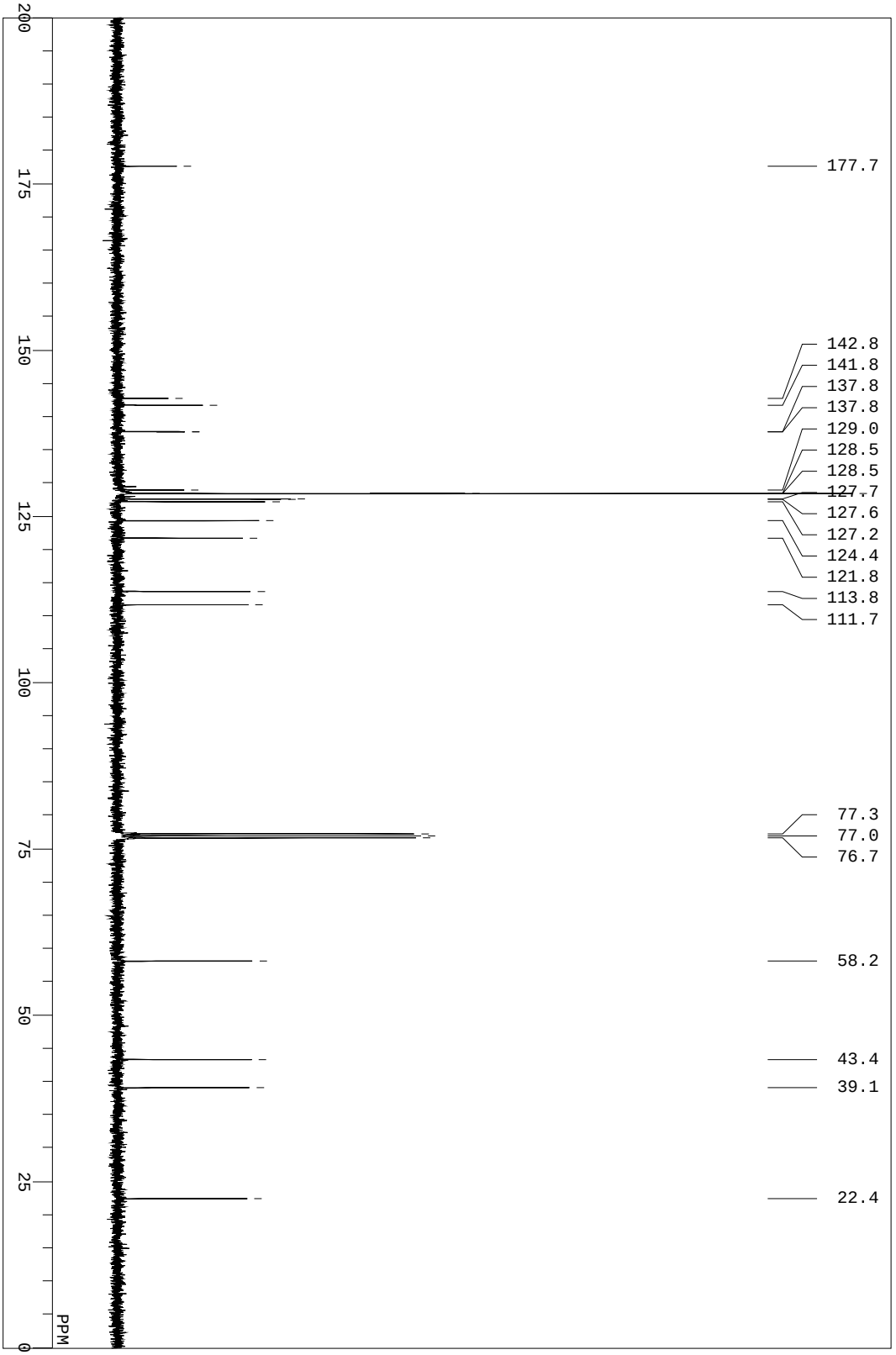

10
8
6
4
2
0
PPM
11.7
1.0
2.0
1.0
1.0
2.1
3.2
7.34
7.21
7.05
6.98
6.97
6.97
6.96
6.95
6.94
6.45
6.44
6.43
6.43
6.42
6.41
6.40
3.56
3.55
3.54
2.18
2.16
2.16
2.14
2.14
2.12
2.11
2.10
2.10
2.09
2.09
2.09
2.08
2.07
2.06
2.06
2.05
2.04
2.04
2.03
2.02
2.01
0.87
0.85
0.84
0.00
O
Et
N
CHPh2
4h

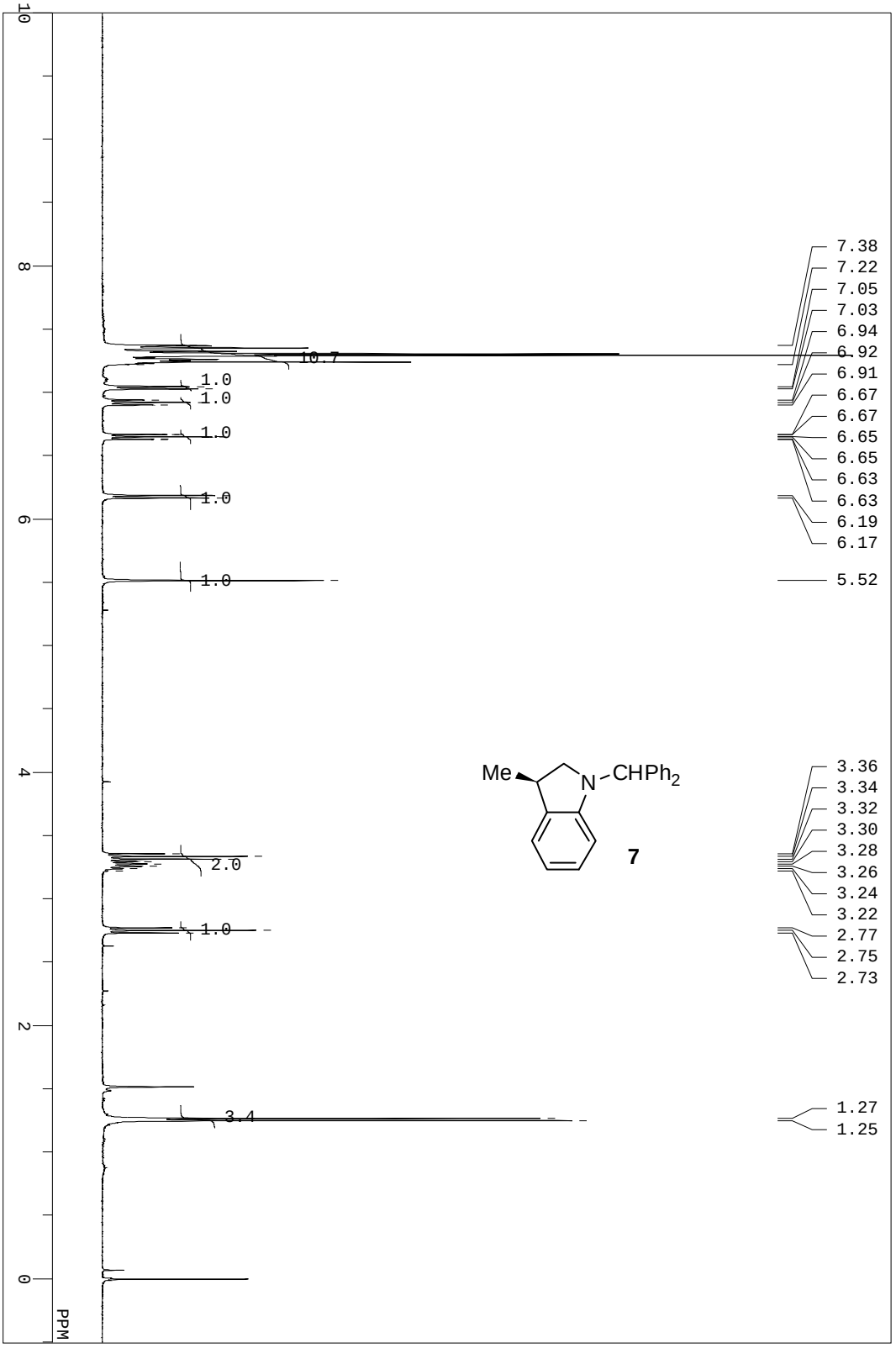

200
175
150
125
100
75
50
25
0
PPM
178.0
143.3
137.9
128.9
128.5
128.5
128.4
127.6
127.6
127.2
123.7
121.9
111.7
77.3
77.0
76.7
58.0
46.2
24.0
9.8

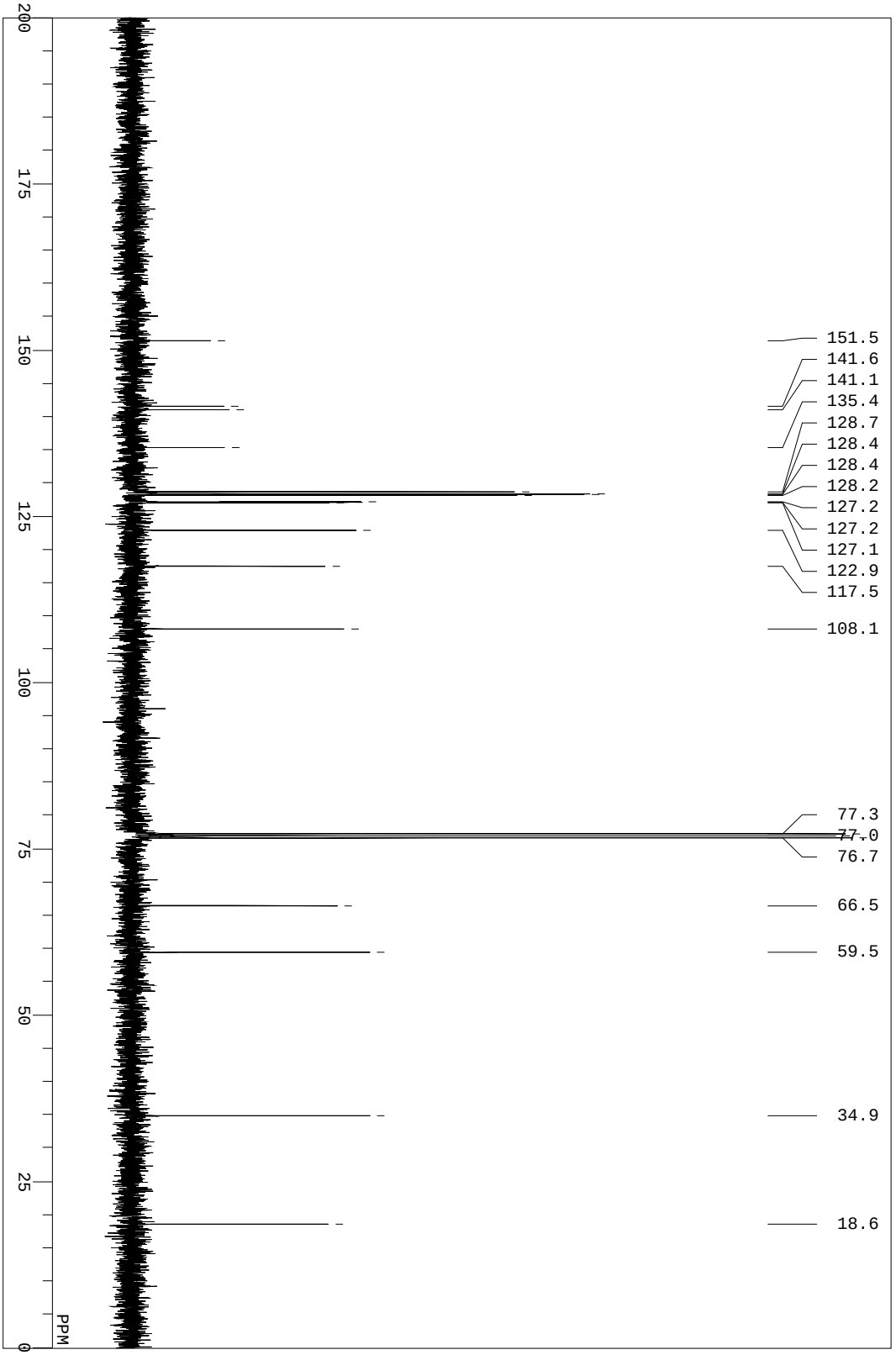

10
8
6
4
2
0
PPM
7.32
7.13
7.09
7.05
6.93
6.88
6.73
6.71
6.26
6.25
6.24
6.24
6.23
3.89
3.88
3.87
3.86
3.46
3.45
3.43
3.42
3.30
3.28
3.26
3.25
1.55
0.00
13.6
3.1
3.0
2.0
1.0
1.0
1.0
1.0
O
Bn
N
CHPh2
4i


200
175
150
125
100
75
50
25
0
PPM
176.9
143.0
137.8
137.2
136.9
129.8
128.5
128.5
128.3
128.2
128.1
127.6
127.3
127.2
126.6
124.2
121.7
111.8
77.3
77.0
76.7
57.8
46.7
36.4


10
8
6
4
2
0
PPM
12.0
1.0
2.0
1.0
2.1
1.0
1.0
1.1
3.1
7.34
7.23
7.03
6.98
6.90
6.46
6.44
4.86
4.76
3.69
3.68
3.67
3.66
2.89
2.88
2.85
2.84
2.49
2.46
2.45
2.43
1.76
O
N
CHPh2
4j


200
175
150
125
100
75
50
25
0
PPM
177.7
142.8
141.8
137.8
137.8
129.0
128.5
128.5
127.7
127.6
127.2
124.4
121.8
113.8
111.7
77.3
77.0
76.7
58.2
43.4
39.1
22.4


10
8
6
4
2
0
PPM
7.38
7.22
7.05
7.03
6.94
6.92
6.91
6.67
6.67
6.65
6.65
6.63
6.63
6.19
6.17
5.52
3.36
3.34
3.32
3.30
3.28
3.26
3.24
3.22
2.77
2.75
2.73
1.27
1.25
10.7
1.0
1.0
1.0
1.0
1.0
2.0
1.0
3.4
Me
N
CHPh2
7


200
175
150
125
100
75
50
25
0
PPM
151.5
141.6
141.1
135.4
128.7
128.4
128.4
128.2
127.2
127.2
127.1
122.9
117.5
108.1
77.3
77.0
76.7
66.5
59.5
34.9
18.6